SAJOUS'S

ANALYTIC CYCLOPEDIA

OF

PRACTICAL MEDICINE

BY

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ASSISTED BY

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WITH THE ACTIVE CO-OPERATION OF OVER

ONE HUNDRED ASSOCIATE EDITORS

SEVENTH

ENTIRELY REVISED AND GREATLY ENLARGED

EDITION

Illustrated with Full-page Half-tone and Color Plates and Appropriate Cuts in the Text

VOLUME ONE

PHILADELPHIA

F. A. DAVIS COMPANY, PUBLISHERS

1919

PRESS OF
F. A. DAVIS COMPANY
PHILADELPHIA, U. S. A.

PREFACE

TO THE SEVENTH EDITION

It is perhaps unnecessary to inform the reader, so apparent is the fact, that the present edition amounts practically to a new work. So extensive have been the additions over and above all the preceding editions that, exclusive of the index, over 2000 pages were required to accommodate them. These additions have consisted mainly of a large number of entirely new articles on practical medicine, surgery, therapeutics, gynecology, obstetrics, dermatology, ophthalmology, laboratory diagnosis, etc., and of completely rewritten and enlarged articles. As the reader can readily see also, the work appears in different type—additional evidence to the effect that all opportunity to introduce any amount of new matter was afforded to the editor's distinguished collaborators.

The purpose of the work remains what it was designed to be from the start, *i.e.,* to assist the practitioner in his daily labors by enabling him to obtain all the *practical* information available of value in the vast domain of Medicine in all its applied branches. What this means in the present connection can be readily surmised from the fact that the clinical index alone, which includes only the remedial measures mentioned in the body of the work, exceeds 200 pages. This clinical index, which has for its purpose to afford a ready reference in emergency work, and is intended to be kept on the physician's desk, includes over 18,000 hints in the field of applied therapeutics, including all the modern methods of chemotherapy, vaccine therapy, organotherapy, serum therapy, psychotherapy, etc.—an aggregate unequaled so far by any medical work of its size.

The presentation of such an array of remedial resources, besides considerable material covering the other classic subdivisions of disease: symptomatology, diagnosis, pathology, etiology, etc., was rendered possible only by a widespread search into the literature of each of the subjects treated. This labor, undertaken by the central staff, is represented by the small-type matter inserted in each article. This small-type text serves also to present confirmatory evidence of the views incorporated in the large-type articles, and to furnish the reader what newer views or suggestions of practical interest and of special value the literature of the last ten years contains.

Besides the regular drugs of the Pharmacopeia in actual use, there have been added a number of proprietary drugs which have received the sanction of the profession at large or of the Council of Pharmacy. So many of these agents are commonly employed nowadays that to omit them altogether is to deprive the reader of considerable therapeutic assistance.

Again, to further facilitate the work of the practitioner, there have been added to the subject-matter a series of articles in small type, in which are given in succinct form the least complicated of the clinical microscopic and chemical diagnostic methods, without which the modern physician cannot fully do justice to his professional work. Such all-important topics as albuminuria, acetonuria, etc., are ranked with the general articles, however, and treated in full.

Expressions of gratitude are due to the editor's associates and collaborators, all masters in their chosen field. Had it not been for their generous co-operation in the preparation of the general articles, so comprehensive a work could not have been brought to a successful issue.

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SAJOUS'S ANALYTIC CYCLOPEDIA *of* PRACTICAL MEDICINE

A

ABDOMEN, SURGERY OF.—Abdominal surgery in its wide sense includes a great variety of operative procedures which are based upon the same general principles as the ones which are included in this article, but which have been left to contributors in the other departments: all of the external hernias, a good part of renal surgery, the surgery of the abdominal walls, and all of the pelvic surgery of the female.

This article takes account of that part of abdominal surgery which includes hollow and solid viscera, the former comprising the various parts of the alimentary tube between the diaphragm and the brim of the pelvis, all biliary and pancreatic ducts and the gall-bladder. The solid viscera belonging to this series of articles comprise the liver, spleen and pancreas only.

There is a general sameness of the alimentary canal in these various parts which leads to more or less correspondence between operations done at the different levels of this tract. Operations of the biliary ducts and gall-bladder also have many points in common, and they resemble in a way the operative resources that are employed for the genitourinary passages.

We propose to consider the special features of abdominal surgery in two ways: first, as a series of typical operations which are intended to correct certain diseased states, and then from the other direction as a series of diseased states to be relieved by operative procedures of various kinds. It seems therefore of advantage to consider the typical operations for the stomach, small and large intestines and biliary passages as operations which are in a way applicable to all surgical conditions of these organs. Surgical diseases of the peritoneum, appendix, liver, spleen and pancreas require separate consideration in detail, because of the relative absence of typical operations, making the treatment more or less individualized for each case.

THE FOURTH ERA IN SURGERY.—In abdominal surgery we have perhaps the best field for object lessons relative to the new fourth or physiologic era in surgery. The first era in surgery was the heroic, under which practically no abdominal surgery was done. In the second or anatomic era of surgery, abdominal

operations were in general so dangerous that few were attempted, excepting in cases of great emergency, and usually with a fatal ending. The third or pathologic era of surgery was based upon the studies of Pasteur and of Lister. Aside from its technique of preventing the development of bacteria in wounds, it included the idea of removing all products of infection with painstaking care.

Notwithstanding the injury that was done to patients by surgeons carrying out the principles of this era, abdominal surgery made its first great advances. Detailed attention was given to the deliberate disposal of products of infection found within the peritoneal cavity, and little or no attention was paid to the natural resistance forces contained within the patient himself. There was an enormous waste of such forces, in fact, in our abdominal surgery of the pathologic era.

The entirely modern or physiologic era is based upon the studies of Metchnikoff and Wright, and includes the principal idea of allowing the patient to retain his natural forces in such a way as to gain control of infections. Metchnikoff and his followers taught us that certain cells of the blood and lymph circulatory systems not only disposed of bacteria daily under normal conditions, but that these cells were increased in number rapidly to meet emergencies of infection. These investigators showed also that bacteria were destroyed by certain fixed body cells. Wright and his followers showed further that, in the presence of an infection, several kinds of antibodies were elaborated in the animal economy, and these antibodies lent their aid in removing infections and in destroying certain toxins that were produced by bacteria. The principles of this fourth or physiologic era of surgery brought us face to face with the problem of operating in such a way as to leave the patient in the very best condition for managing infections himself with his own phagocytes and antibodies, and led to a revolution in methods, forcing us to drop out of our technique such parts of the system of the third or pathologic era as interfered with the ability of the patient to produce phagocytes and antibodies.

For instance, a prolonged and painstaking operation for removing all of the pus from the peritoneal cavity so shocked the great vasomotor centers of the patient that they were palsied, and unable promptly to take up the work of conducting the manufacture of phagocytes and antibodies, with which the patient himself could dispose of the products of infection much better than the surgeon could do it in his crude mechanical way.

Unnecessarily prolonged operations acted in precisely the same way; and where we had thought best to expend a half-hour in carrying out the theories of the pathologic era in surgery, we may now expend five minutes under the principles of the physiologic era.

> Shock is produced more readily by manipulation of the abdominal viscera than by gross injuries, when animals are fully anesthetized, especially when the anesthetic used is chloroform. The parietal peritoneum and the peritoneal mesenteries are especially sensitive to shock under manipulation. Mammery and Symes (Brit. Med. Jour., vol. ii, p. 790, 1908).

A long period of anesthesia was commonly required for thorough work under the principles of the third era, but we now know, from our experiments upon animals, that individuals profoundly under the influence of alcohol, or of ether or of chloroform, temporarily lose resistance to infections, and some acute infections which would not gain headway under a few minutes of anesthesia may seize the opportunity to gain ascendancy if the anesthesia is prolonged for an hour or two. Bulky or complicated drainage apparatus, acting as a foreign body, further produce derangement of function of the vasomotors in such a way as to prevent the patient from manufacturing his phagocytes and antibodies. We are just entering, then, the era in which the greatest degree of success is to follow our operative procedures within the abdominal cavity.

ANTEOPERATIVE MANAGEMENT.—Aside from the general principles which govern the preparation of a patient for any major operation, certain special requirements are indicated which lessen the operative risk, and the tendency to postoperative complications in abdominal surgery.

Postoperative pneumonia, for instance, will occur less often if we make careful choice of the anesthetic for any given case, and if we make this period of anesthesia as short as possible, on account of the known tendency of some acute infections to shoot ahead when the patient is under the influence of ether or chloroform. Some operators will choose nitrous oxide and oxygen in cases in which this phenomenon is anticipated. In some feeble patients, or patients with complications of disease of vital organs, spinal anesthesia according to the Jonnesco method is desirable.

Preoperative intestinal asepsis can only be approximated, but for most practical purposes a good purgative given within twenty-four hours of operation will suffice. If the stomach itself is to be operated upon, further steps in the direction of asepsis are required, and we wash the stomach out very thoroughly with saturated boric acid solution just in advance of operation. This is done most comfortably, as a rule, after the patient is under the influence of the anesthetic, and by means of the common siphon tube. After the alimentary tract has been cleansed by purgatives, it is important to give only the simplest articles of food and drink in advance of the operation, but we must avoid having a patient abstain in such a way as to become unduly weakened. Patients who are accustomed to dieting may sometimes be placed on special diet to advantage for a few days in advance of operation, but the physical effect of placing a patient on diet for any length of time is apt to be such as to counteract any good effect.

In general a short period of rest in bed before an operation is of advantage, but if this time extends beyond twenty-four hours, excepting for patients who are already in bed with some severe abdominal complication, the apprehension and introspection of the patient with a negative imagination, in advance of operative procedures may be disastrous, and has even gone to the point of allowing the patient to develop suicidal impulse. For patients who are not already in bed from necessity, the author prefers to have as short a period of preparation as expediency would suggest,

not more than twenty-four hours as a rule. There are many instances in which the patient needs special medical treatment in advance of operation, because of some defect of the heart, lungs, or kidneys, but under such circumstances with most patients it is best not to tell them of the date set for operation far in advance, up to which they are to be led.

Anteoperative narcosis is undesirable for one chief reason shown by Cantacuzene in his experiments with animals subjected to the influence of opium after infection. This author showed that narcotized animals rapidly succumbed at the time when another series subjected to the same infection, but not narcotized, were meeting the infection. Arrangements should be made in advance of operation for maintaining the animal warmth of the patient with woolen garments or blankets, and it is best to have a good circulation of air in the operating room. In an overheated operating room with closed windows and doors the surgeon himself may be extremely uncomfortable, and feeling the need for oxygen, and we assume that the patient at the same time suffers the same depressing influence in addition to the shock of the operation. Experiments with animals have shown that the peritoneum is not injured by exposure to air currents and to low temperature as much as it is injured by contact with gauze antiseptic solutions, or by rough handling. The author believes that the temperature and air circulation of the room most agreeable to the surgeon is at the same time most beneficial to the patient. Asepsis is to be begun where possible before the operation with a general bath, and particular attention given to the preparation of the umbilical region.

The skin in the field of operation may be well prepared in the common way by shaving, then scrubbing with green soap, which is washed off with a weak bichloride of mercury solution, and a pad of gauze wet with this solution is placed in contact with the wound for a few hours. A recently introduced and very effective way of sterilizing the skin consists in simply painting it over with a 2 per cent. solution of iodine in benzin after shaving.

The need of aseptic surroundings relating to the preparation of the operating room need not be discussed in this article. Asepsis on the part of the operator is met by the wearing of a sterile gown and cap and a mouth guard of gauze, because with every breath, and particularly in the course of conversation during an operation, bacteria are projected from the mouth of the operator over the field of the wound.

The hands and forearms may be prepared simply by scrubbing with green soap, and then in a weak solution of bichloride of mercury. This destroys practically all of the bacteria which are likely to cause trouble. Latent colonies of bacteria which work out of the epithelium of the hands in the course of an operation are generally dormant colonies which are managed by the blood-serum or tissues of the patient safely. The use of rubber gloves in abdominal surgery is particularly undesirable; first because they interfere with the nice sense of touch required for separating adhesions, or for doing rapid suturing. The operator wearing rubber gloves is apt to require longer incisions which allow him to work by

sight, and this is not in harmony with the principles of the physiologic era in surgery.

The peritoneum protects itself so well if given fair opportunity that we do not need to apply the extreme degree of asepsis that would be needed in opening the knee-joint or the meninges of the brain, but it is well for assistants who are not engaged in separating adhesions, or in applying sutures, or in hunting for structures within the abdomen, to wear rubber gloves. One can do a much higher class of operative work within the peritoneal cavity where nice sense of touch is not interfered with; and the greater length of time required in operating where rubber gloves are used and the longer incisions counterbalance the benefit of such asepsis as would be gained through the use of the gloves.

> In more than half of the cases of chronic suppuration in the pelvis the pus is sterile at the time of operation, showing that sterilization of the infected focus takes place automatically within a reasonable time in the majority of cases. H. S. Crossen (Surg., Gynec., and Obstet., Oct., 1909).

It has been shown experimentally with Petri plates in the operating room that large numbers of bacteria are constantly falling into every open wound, no matter what precautions have been observed in advance. These bacteria are for the most part disposed of in the patient's tissues and blood- and lymph-vessels; but the longer the incision and the greater the length of time during which any given wound remains open, the more bacteria fall into the wound from the air.

If one can work more quickly and through shorter incisions with bare hands, he naturally makes better asepsis of the wound, provided that his hands have been well prepared in advance.

> The recent reawakening of iodine disinfection of the surface in abdominal surgery is fraught with danger. In animal experiments (rabbits), very small amounts of iodine injected intraperitoneally will produce in a short time abundant layers of fibrin and firm membranes and bands between the intestines. The effect is to a certain degree specific, in contrast to that of turpentine. The writer injected intraperitoneally in a dog 20 drops of the tincture of iodine, dissolved in 80 c.c. sterile saline solution, and found after forty-eight hours, in the region of the liver and stomach, abundant fibrous adhesions. There were no adhesions in the region of the small intestine. The abdominal cavity in the human subject, on the other hand, inclines especially to adhesions, particularly from a moderately specific irritation, as from gonorrheal infection. The writer has, since the introduction of iodine disinfection, in about 70 cases of appendicitis, simple or complicated with abscess or peritonitis, 6 times found ileus from kinking or adhesions. This was unusual before the use of iodine for this purpose. Of about 300 cases of appendicitis in 1910 and 1911, before the introduction of iodine disinfection, there were only 5 cases of mechanical intestinal obstruction. He concludes that eventration of the intestines directly upon the browned skin should be absolutely avoided. They should be laid on interposed layers of gauze moist with saline solution. Whether this will be sufficient to prevent harmful effects from the iodine must be determined by further observations. Propping (Zentralbl. f. Chir., Bd. xxxviii, S. 661, 1911).

Instruments may be sterilized by dry heat in the oven, by immersion in 95 per cent. carbolic acid, or in the more common way by boiling in water for fifteen minutes. In the

later case bicarbonate of soda in the proportion of a teaspoonful to a quart of water is added to prevent the rusting of instruments. The carbolic acid preparation is particularly suitable for small, sharp, delicate instruments, and does not interfere in any way with their edges. The carbolic acid which clings to them on removal is instantly neutralized by immersion in alcohol.

INSTRUMENTS AND APPARATUS.—**Scissors.**—There are very few intra-abdominal operations which cannot be performed from first to last with a pair of scissors and a couple of needles and no other instruments whatsoever. In adding other instruments which give special facility in certain operations it is well to remember this statement, and it will avoid the multiplicity of instruments which are frequently used to the patient's disadvantage or injury, as may be observed often enough. The form of scissors which the author prefers is the ordinary French locked type, five or six inches long, with one sharp point and one blunt point, and kept very sharp. The preference for scissors over scalpel is based upon the fact that small blood-vessels seem to ooze much less after division with the scissors than with the scalpel. This is possibly due to contraction stimulated by the character of the cut made by the scissors, but there is no interference with primary union of the tissues subsequently, according to observations extended over a series of years.

Needles of the Hagedorn type will suffice for practically all abdominal work, and needles threaded with catgut slipped under bleeding vessels readily take the place of the artery forceps without loss of time, with a rather greater degree of accuracy, and with less crushing of tissues. For intestinal or gastric suturing the author prefers a needle that is considerably larger than the one that is commonly used, for the reason that it carries a suture of greater diameter, and a suture of fairly large diameter does not cut out of the tissues so readily as an extremely fine suture when subjected to tension. The custom of using a very fine needle and silk is based upon the idea of causing the least degree of operative damage and avoidance of leaking of contents of the hollow viscera, but it is not based upon our observations of the extent to which the mucous membrane will plug fairly large punctures, or our knowledge of the greater security of tissues sutured with a strand large enough to bind without cutting.

Retaining Apparatus.—The author is in favor of depending upon his fingers, and those of assistants, rather than upon clamps and other retaining apparatus in abdominal work; but this is because his methods were acquired while many of the proficient clamps which facilitate these procedures were in the course of development, and which gave mechanical advantages which seemed attractive, but which were sometimes observed to be injurious. Rubber-covered clamps of various forms, if carefully used, allow one to work speedily. One may not make such accurate adjustments or such regular insertion of sutures if he disposes of mechanical adjuncts, and yet in cases where he can work quite as quickly without them the balance of advantage is in favor of the gentler method. Temporary steadying sutures may some-

times be employed in addition to the fingers in order to maintain a viscus in a certain position while operation is being performed, and these are liable to do less harm than steel instruments in the peritoneal cavity. The author has employed most of the mechanical devices described for facilitating operative work upon the stomach and bowel, but has dropped most of them, excepting the Murphy button, in favor of simple methods of suturing, and the button is not used nearly as often now as it was a few years ago.

Drainage tubes for the most part should be small, as otherwise they play the part of a foreign body in the abdominal cavity, and this is resented by the peritoneum. In 1895 the author described, in his book on the subject of appendicitis, a drainage wick which would take the place of drainage tubes in most places in the peritoneal cavity, and which would cause very little offense to the peritoneum. It consisted of gauze rolled loosely in a covering of gutta-percha or of rubber dam, very much as one rolls a cigarette, but leaving one end of gauze protruding. This soft, flexible drainage wick acts by capillarity, adapts itself to bends and angles, and suffices for most purposes of abdominal drainage, provided that one understands the principles of capillary drainage, and keeps a good mass of fresh gauze upon the abdominal wall in such a way as to maintain the capillary power of the wick.

Gauze drains not protected with an inoffensive covering are quickly filled with lymph-coagula poured out from the peritoneum in response to their irritating presence, and they become fastened to tissues in such a way that on removal they may draw loops of bowel into angulation. Where a very long drain is required, as from the cystic duct or from the bottom of the pelvis, the same principle may be applied by using an ordinary flexible-rubber drainage tube or catheter split throughout its entire length on one side, and the wick of absorbent gauze carried loosely through the lumen of the tube. It is very seldom at the present time that one will need to use any gauze packing in the peritoneum cavity; but if such a calamity does arise, less harm is done if the gauze is covered with an apron of gutta-percha tissue or rubber dam to keep the bowel from becoming adherent, thus carrying out in a way the principle of the protected drainage wick. For patients with very heavy abdominal walls where pressure might nearly close the wick drain with its cover of rubber dam, or of rubber tubing, sheet lead is a useful part of our apparatus. Sheet lead can be cut with the scissors into strips of any desired width or length, and this strip doubled upon itself carries between the two arms a drain of absorbent gauze. The end of lead projecting upon the external abdominal wall can be bent over to avoid the danger of the drain slipping within. Lead seems to be quite as benign as rubber or gutta-percha tissue, and is accepted kindly by the tissues, excepting where it projects to some distance within the abdominal cavity, in which latter case it presents a more rigid and objectionable foreign body.

Suture Materials.—The choice of suture materials in abdominal surgery is extremely important.

For ordinary ligating of vessels, and for suturing of the peritoneum

where adhesions are to be avoided, very simply prepared catgut is preferable, and excepting for large vessels a catgut which would be absorbed in forty-eight hours possesses advantages, because any suture material for the peritoneum which remains for two or three days is prone to cause, by its irritating presence, a line of peritoneal lymph-exudate followed by annoying adhesions. This is in accordance with the well-known action of the peritoneum in walling in any object which is a source of irritation. While such adhesions may be absorbed later, and may not be in a position to cause much annoyance, nevertheless there are many thousands of patients today suffering to some degree from adhesions of the omentum or bowel to the anterior abdominal wall, in cases where this complication could have been entirely avoided by the use of very fine, quickly absorbed suture material, which would not have caused the pouring out of much lymph by the peritoneum. Peritoneal margins united with the finest of sutures become adherent so quickly that there is no real need for any suturing which will last for more than twenty-four hours in the parietal peritoneum of the abdominal wall, or in other places where strong permanent adhesions are not purposely induced.

For suturing the cut margins of bowel or stomach for the purpose of preventing hemorrhage, and of closing of tissues against infection, small chromic catgut in the place of simply prepared catgut is desirable, for it resists digestion when in contact with the secreting glands of these organs longer than simply prepared catgut. Simply prepared catgut, when in the secreting glands of the stomach or bowel, may be liquefied in a very few hours, and chromic catgut in this position will do no harm, because it is at a point where adhesions are purposely secured.

Linen thread and silk are used in the positions where we wish snug apposition of tissues until firm adhesions have been formed, or cut structures of the stomach or bowel have united. For closing all parts of the abdominal wall we may dispose of any suture material, excepting the very fine, simply prepared catgut for the peritoneal layer and skin, and chromic catgut for the anterior and posterior sheaths of muscles; but, in place of chromic catgut where a lasting, yet absorbable material is desired, the author is very fond of kangaroo tendon. It is remarkably benign in the tissues, which receive it with such a degree of toleration that large strands are carried readily, and the kangaroo tendon lasts in the tissues for a longer time than chromic catgut, unless the latter is prepared in a way which makes it so hard as to be irritating.

POSTOPERATIVE TREATMENT.—The patient on being returned to bed should have wool next the skin and hot bottles at the extremities, even though not much shock be present, for shock is present to some degree after almost any abdominal operation, due to stimulation of the afferent nerves of the brain and cord centers, with more or less lack of vasomotor power. There is apt to be more or less perspiration from leaking sweat-glands when the patient is placed in bed, and any undue exposure at this time may lead to a chilling which would be inducive

to postoperative pneumonia. For the first twenty-four hours approximately the disturbance of the intimate ganglia of the bowel will usually result in derangement of function of the bowel so that any food material is apt to undergo fermentation instead of digestion, and the toxemia from such fermentation may be very injurious, and might give rise to serious complications.

Thirst is inseparable from the postoperative period, and **hot water** given in teaspoonful doses frequently will partially allay the thirst, and supply all the real needs of the stomach for some hours after the operation. Patients are very urgent at times in their demands for cold water or ice after an operation, but cold water has a distinct tendency to increase vomiting, and ice in the mouth produces the same reaction that cold does upon the skin, as one observes after making snowballs: the hands become red and irritated, and in the same way the mucous membrane of the mouth and pharynx becomes irritated, if the patient is allowed ice or ice-water, excepting in the most minute quantities.

> It has been the practice with surgeons after abdominal operations to withhold water by the mouth for twenty-four hours, or until the patient is free from nausea and vomiting. During this time the thirst is distressing.
>
> Some surgeons have for several years administered water by the rectum in small quantities to allay thirst; but the routine method of injecting a large quantity of saline solution (0.6 per cent.) for the prevention of thirst after abdominal operations was first resorted to in the Johns Hopkins Hospital. The procedure consists in the **injection of** a quart of **normal saline solution into** the **lower bowel** immediately at the close of the operation and while the patient is still under the influence of the anesthetic. The patient is elevated to the moderately high Trendelenburg posture, a stiff rectal tube is inserted well up into the sigmoid flexure, and the fluid slowly poured into a glass funnel, which is held 3 or 4 feet above the level of the patient's buttocks.
>
> John G. Clarke reviewed the charts of 100 abdominal section cases which had not and 100 cases which had received the saline enemata; he was able to report the most gratifying results not only in the alleviation of thirst, but also in the reduction to a minimum of vesical irritability, which is so common in operative cases. W. M. Taylor (Memphis Med. Monthly, Feb., 1897).
>
> Saline rectal infusion is a most valuable means of relieving thirst so frequently complained of after abdominal operations. A. S. Morrow (Diagnostic and Therapeutic Technic, p. 509, 1911).

Diet.—The first food to be borne after the hot-water period is passed is liquid diet and predigested milk, or fermented milk of several kinds, and broths are usually well borne. In two or three days, if the temperature and other vital signs are fairly normal, a more liberal diet will allow the patient to regain strength more rapidly. Meteorism, which is usually present to some extent, with or without colic, because of the disturbance of the sympathetic ganglia of the abdomen, may be relieved ordinarily if stimulating enemata are given; but for the most part it is well to leave the patients pretty much alone, without attempting to do too much for them during the first twenty-four hours after an abdominal operation. Many times the author has asked patients what they most desired during the first day after an abdominal operation, and the common answer has been that their greatest desire was to be left alone.

Opiates.—There is a general tendency to give opium in some form after abdominal operations, if the patient is in pain, but we must remember the specific action of opium in lessening the resistance to the spread of infection immediately after an operation, and not apply mistaken efforts at kindness in wishing to quiet the patient's pain. There are some patients of nervous temperament who suffer so much and who are so restless that they tire themselves out with fretting, if we do not give opium in some form.

Consequently the resource is one that we may be obliged to use, but it should not be used excepting with full knowledge of its danger. It is the author's habit to tell patients in advance of operation that they are going to suffer a great deal afterward from colic, nausea and pain, but that they will arrive at a comfortable stage soon afterward. The effect of this statement to the patient has never, so far as the author knows, deterred anyone from having an operation done, as there is the natural feeling of pride in being able to meet such conditions, and the patient, expecting a good deal of trouble immediately after operation, and prepared for it, is frequently enough surprised to find it so much less in degree than had been anticipated.

Insomnia is so dependent on stomach and bowel disturbances that the two belong closely in association. Insomnia which is dependent upon the disturbance following an operation is not so distressing if the patient has a good nurse who suggests quiet in all of her movements, and who does not allow avoidable disturbances to keep the patient awake. Sleep will be established frequently in a natural way by the third night. Part of this insomnia at night is due to the fact that patients doze off at various times during the day, and really get during the twenty-four hours about all of the sleep that is necessary. A number of ordinary hypnotics, avoiding the opium preparations, will give some relief, and this is a matter which must be left to the judgment in individual cases rather than stated in the way of a general rule.

Should the patient be allowed to leave his bed early? The suitable cases after abdominal section are those in which traumatism within the peritoneum is slight. Great care is necessary in the selection of these cases, because union of the abdominal wound may not be strong enough to withstand the intra-abdominal pressure of sneezing or coughing even so late as the twelfth day. Vance (New York Med. Jour., Feb. 16, 1907).

The writer allowed 100 patients to rise in the course of the first week after laparotomy, 13 on the first day, 16 on the second day, 21 on the third, 30 on the fourth, 10 on the fifth, 8 on the sixth, and 2 on the seventh day, and has been much pleased with the results. Thrombosis occurred in 3 cases, but soon subsided; the condition was evidently responsible for it. It is advisable to be cautious in allowing patients to get up very early when they had unduly high temperature or disturbances in circulation in the legs or pelvis, but under other conditions it is an important advance in the treatment. F. Cohn (Zentralbl. für Gynäk., Sept. 19, 1908).

No matter what the lesion or how weak the patients, the writer has them recover from ether in the sitting posture by means of a bedrest. He keeps them in this posture for about twelve hours, and then allows them to lie down and turn in any position that is comfortable. They sit up again with a bedrest practically all the next twenty-four

hours. On the third day, if strong, but anyway on the fourth day, he has them in a chair. On the fourth or fifth day they walk around. From that time on they walk or sit up with their clothes on during the day, leaving the hospital usually from the tenth to the fourteenth day. Chandler (Albany Med. Annals, Feb., 1908).

Report based on results in 164 cases of laparotomy which were allowed to leave the bed between one and three days after laparotomy. Of these, 50 were for hernia; 56 for interval appendicitis; 20 for acute appendicitis; 7 for cyst of the ovaries; 4 for uterine myoma; 8 for Alexander Adams's operation; 3 for cholecystectomy; 3 for gastroenterostomy, and 4 for enteroanastomosis. The rest were instances of exploratory laparotomy. Of all these cases, 1 only suffered from thrombosis, and that to a mild extent. The formation of a firm cicatrix occurred promptly in all. Perfect narcosis without vomiting or other untoward effects, rapid operating and but little loss of blood, firm and close fascial suture, and aseptic healing of the wound are essential to success. Kummell (Zentralbl. für Chir., Bd. xxxv, S. 4, 1908).

The writer does not believe in keeping patients upon whom laparotomy has been performed several weeks in bed. If there are no indications of fever he is inclined to let them get up after a few days, dependent greatly on the patient's own desire. When there is fever, however, the patients are kept in bed, as early rising may then do harm. The objections usually urged, dangers of secondary hemorrhage, breaking open of the wound, and embolism, are theoretical rather than practical. Hartog (Berl. klin. Woch., March 15, 1909).

We are still too much tied down in this respect by the traditions of the old, bad system of septic surgery with its suppurating wounds. When a wound is full of pus no relaxation can be allowed, but aseptic wounds are a new development and must be judged by totally different standards. So far as these are concerned, it is time that we discard ancient authority and think out the matter for ourselves. In the first place, a clear distinction must be drawn between allowing a patient to be lifted quietly out of bed and placed in a comfortable chair with abundance of cushions and pillows for a few hours each day, for the sake of having his meals in comfort or for other reasons, and letting him get up and get about by himself, doing whatever he thinks fit. The latter is opposed, if for no other reason than that it is impossible to guarantee the patient against accidents. Moullin (Clin. Jour., March 16, 1910).

POSTOPERATIVE COMPLICATIONS.—Shock when severe in degree requires special treatment in addition to the customary methods for retaining the body heat and keeping hot bottles at the extremities. **Elevation of the foot of the bed** temporarily allows the heart to work with less effort, but we have to be guarded about suddenly lowering the foot of the bed at any time while the patient is still in a condition of shock. The patient at this time may be suffering from one of two kinds of anemia: anemia due to lack of vasomotor power and perhaps also anemia due to direct loss of blood. For the anemia due to loss of vasomotor power secondary to derangement of function caused by disturbance of the sympathetic ganglia of the abdomen **strychnine** is indicated, and should be given hypodermically in doses of from a thirtieth to a twentieth at intervals of about four hours.

For the anemia due to actual loss of blood the indications are for supplying the loss of blood temporarily, and this is done either by direct **transfusion of blood** or more commonly by intravenous infusion of **normal saline solution.** In cases in which we have

both kinds of anemia present at the same time the use of the strychnine may be quickly transitory and injurious, unless we have first by transfusion or infusion given the heart and blood circulatory system the mechanical advantage of possessing a full complement of fluid.

Adrenalin or **digitalis** are powerful stimulants, but they stimulate the heart out of proportion, and are very transitory in effect, and unless given with great caution may lead to overstimulation, especially if given in conjunction with strychnine. Overstimulation will be followed by secondary shock coming on a few hours after apparent recuperation from the first evidences of shock. **Bandaging the legs** firmly in order to drive out the blood in part and give the heart less work is, like elevation of the foot of the bed, a resource of temporary value, but we need to be guarded about removing the bandages before recuperation from the condition of shock is well established.

> The best method of administering the adrenal principle is by continuous rectal injection in **saline solution,** 1 dram of solution of **adrenalin** to a pint of the saline solution—that is to say, 1 in 160,000; the temperature of the liquid should be between 108° and 112° F., and it should be allowed to flow in not faster than at the rate of 1 pint an hour. A. J. Walton (Lancet, July 11, 1908).
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> **Adrenalin** will raise the blood-pressure in normal animals in every degree of shock, with the medulla cocainized, or in the decapitated animal. It is rapidly oxidized by the solid tissue and by the blood. Its effect is fleeting; it must, therefore, be given continuously. By this means the circulation of a decapitated animal was maintained ten and a half hours. G. W. Crile (Med. News, Nov. 29, 1902).
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> Hypodermic injections are absorbed very slowly in the blood-stream during severe shock, but intravenous injections of the adrenal principles, **adrenin,** etc., or of **pituitary extracts,** raise the blood-pressure to a greater extent than in the normal state, a single injection of an extract of the posterior lobe of the pituitary influencing arterial tone for upward of an hour, *i.e.,* long enough to produce recovery in some cases. Mummery and Symes (Brit. Med. Jour., vol. ii, p. 790, 1908).
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> In 3 cases of postoperative shock, the writer injected 1 c.c. of a 20 per cent. solution of the posterior lobe of the **pituitary body** intramuscularly into the patient's arm before the patient had fully recovered from the anesthetic. The effect was almost immediate, and the almost imperceptible pulse soon became large and bounding. This effect lasted from twelve to sixteen hours, and gradually passed off. Not only did the pulse become larger in expansion, but it was also slowed, and whereas it had been irregular it became regular. This effect seems due not only to the action of the drug on the blood-vessels, but also on the heart. The injection was given in conjunction with normal saline by rectum. G. G. Wray (Brit. Med. Jour., Dec. 18, 1909).

Meteorism of extreme degree also appears to depend upon two chief factors: partial paralysis of the muscularis of the alimentary tube due to disturbance of the sympathetic centers, and to fermentation of contents of the alimentary tract caused by saprophytes, which gain ascendancy when the normal control occurring in the course of undisturbed digestion is taken away. The meteorism secondary to mechanical obstruction or of spreading peritonitis includes these same prime factors, but the different forms of this condition require treatment based upon causation in the individual case. The meteorism which is due to simple shock calls for mechani-

cal treatment chiefly, although the fermentation of intestinal contents is relieved to some extent by the use of **subgallate of bismuth** as an intestinal antiseptic, and by the use of the **lactic acid ferment**, consisting of prepared cultures of the *Bacillus Bulgaricus*, which now may be obtained in tablet form, or which may be used indirectly in milk prepared by the action of this bacillus.

Mechanical resources consist, in ordinary cases, of introducing a **rectal tube** to allow the early escape of gas, and by **abdominal massage** applied gently but persistently, beginning at the right side over the cecum and carrying the massage along the entire course of the colon. This order of massage movements seems to relieve distention of the small bowel quite as well as the colon, probably because of the natural tendency toward emptying of the small bowel into the colon. In the presence of severe colic in meteorism, massage would seem to be contraindicated, but it is not, because colic is due to a spasm of the muscularis of the bowel in its effort to contract to the normal caliber, and massage movements seem to give to the bowel the same sense of security that is obtained by a splint in cases of fracture with muscular spasm of the extremities. The author is impressed by the fact that treatment of meteorism of the bowel in this way by massage and by the rectal tube is not commonly appreciated as it should be, and he has very many times afforded decided and lasting relief by these resources.

A hypodermic injection of 1/50 grain of **salicylate of eserine** gives excellent results in cases of tympanites after colotomy. Within fifteen minutes of its injection the patient begins to pass flatus. An enema of **sulphate of magnesium** should then be given. The result is often marvelous. If necessary, the injection may be repeated in six hours without danger. F. E. Taylor (Treatment, Feb., 1906).

Acute dilatation of the stomach belongs to the same category, is probably dependent upon the same causes as meteorism of the bowel, and has practically the same order of complications. In many cases there seems to be selective impression made upon the innervation of the stomach by shock, perhaps because of its proximity to the solar plexus, and dilatation of the stomach occurs out of proportion to dilatation of the bowel. When we recognize acute dilatation of the stomach by the persistent vomiting, distress, and visible distention of the upper left quadrant of the abdomen in excess of distention of other parts of the abdomen, we have the characteristic features of this form of meteorism. In this condition the mechanical features of treatment are all important, and are obtained by placing the patient prone upon the abdomen, with the result of causing constant compression of the distended stomach. With the patient in this position, the stomach tube introduced at frequent intervals, **washing of the stomach with warm saline solution** results in causing the escape of very large quantities of gas. Patients suffering from this condition are not so sensitive to the introduction of the stomach tube as many others, and the immediate relief which is given temporarily often makes them eager for the next introduction of the tube. The important matter is to apply the stomach tube often enough, and this is a point commonly neglected. We must keep the stomach empty of gas and fermenting contents.

In cases in which the patient happens to rebel against introduction of the stomach tube because of highly sensitive fauces we may spray the fauces in advance with cocaine solution, and, if the tube is lubricated with a nice quality of sweet oil to which is added a few drops of wintergreen, the patient, relishing this, will chew the tube for a few moments, and then begin swallowing it. Further advance of the tube is made by the surgeon.

Meteorism due to mechanical obstruction of the bowel is also met with. At the present time we see very much less of dynamic and adynamic ileus than we did a few years ago, when it was common practice to use gauze packing in abdominal surgery. This gauze packing lowered the patient's general resistance, as a foreign body in the peritoneal cavity. It caused excessive exudation of plastic lymph from peritoneal surfaces, and adhesion angulation was a frequent feature in consequence, or if not angulation, the arrest of peristalsis from the involvement of the long segments of the bowel among adhesions.

That form of ileus in which peristalsis progresses violently up to the point of arrest with a rapid production of grave symptoms can oftentimes be relieved by posture. If the patient's hips and legs are elevated upon the back of a chair which has been placed upside down in bed, and gentle massage applied, gravitation will sometimes stop the angulation or kinking of bowel in a few minutes, and it is gratifying to see the whole picture of a desperate case change so rapidly as it sometimes will when this posture resource is being applied, together with gentle massage. Reopening of the abdomen and a search for the point of mechanical obstruction are such very fatal procedures that they must not be employed with much hope of obtaining relief, but some authors hope, which the author does not share freely, to secure an occasional good result by opening the distended bowel by incising it after reopening the abdominal cavity to allow the escape of gas, or by injecting sulphate of magnesia solution through trocar punctures in the bowel. Clinically I think that we may usually observe that when the bowel is opened at any point for the escape of gas it allows the escape of gas only in the immediate vicinity, the paralysis of the bowel preventing the contraction necessary for emptying the lumen at more distant points. Rapid opening of the distended bowel at a point above the obstruction, insertion of a drain to carry off the poisonous contents, and subsequent operation for the relief of the obstruction, after the patient has made some gain, is occasionally successful.

Our resources must be applied promptly in cases of ileus with meteorism, because toxins generated in any part of the bowel which is not emptying itself rapidly lead to a dangerous toxemia, and the colon bacillus particularly increasing in virulent culture in an obstructed or paralyzed part of the bowel may not only cause general toxemia, but may be carried to the kidneys and liver, and there give origin to a train of serious complications discussed under the next heading.

Colon Bacillus Nephritis.—If this continues after relief from the ileus has been obtained, it will require special treatment internally. Five

grains of **benzoate of soda** combined with five grains of **hexamethylenamine** administered at rather frequent intervals, according to the judgment of the physician, will exert a specific influence upon the complication of colon bacillus nephritis which so commonly follows various causes of loss of control over this bacterium. When the benzoate of soda and hexamethylenamin internally do not control colon bacillus nephritis in a satisfactory way, the pelvis of the kidneys may be flushed through a ureteral catheter.

In many cases one may state incidentally that colon bacillus nephritis is often enough present in advance of operation in many abdominal conditions, passing for ordinary nephritis, unless one devises means for determining if the colon bacillus is present, and the author has known of instances in which excellent consultants wished to postpone operation because of the presence of albuminuria, when, as a matter of fact, this albuminuria was due to the presence of the colon bacillus, and to be cured only after removal of the focus of original infection by the abdominal operation. The colon bacillus nephritis which occurs with appendicitis may often clear up rapidly after the operation without any special treatment directed to the nephritis, and the same result may be anticipated in a certain proportion of the cases of colon bacillus nephritis occurring with ileus.

Meteorism due to extension of peritonitis after operation is sometimes treated by the old Clark opium method, which consists in placing the patient profoundly under the influence of **morphine**. It acts by limiting the spread of peritonitis due to peristaltic movements of the bowel, and the loss of resistance on the part of the patient from the shock which goes with peritoneal pain. On the other hand, we have the objection that bacteria increase more rapidly in a patient under the influence of opium. In addition to the beneficial influence of opium in selected cases, the **ice-coil** placed on the abdomen has the tendency to lessen the spread of peritonitis besides limiting the pain.

The author has preferred the principle of turning the blood-current toward emunctories of the bowel, and securing elimination of toxins along with a free watery discharge from the mucosa of the bowel. This is accomplished fairly well by the high rectal injection of an ounce of **alum** in a quart of water. The alum in the bowel produces the same effect that it does in the mouth, causes rapid watery secretion from neighboring glands, and incidentally stimulates contraction of the paralyzed bowel, with emptying of its contents. We might anticipate that alum would have in the bowel an astringent effect, with the tendency to cause constipation, but it has precisely the reverse action, and the great amount of watery exudate which is drawn out in the presence of alum seems to overcome any irritating effect which it might have.

Sulphate of magnesia by high injection has an effect like alum, of causing watery evacuation which presumably carries off toxins, and the influence of sulphate of magnesia is probably due to its hygroscopic nature, drawing fluids from the peritoneal cavity toward the bowel lumen by osmosis. The sulphate of magnesia injection, either alone or combined with **glyc-**

erin, which is also hygroscopic, is perhaps the favored method of obtaining movement when there is any degree of paralysis of the bowel, but the alum injection is much more effective, and will act in cases where paralysis is established to such a degree that sulphate of magnesia would exert no apparent influence. In addition to these rectal injections, a very gentle **massage** is effective in some cases in overcoming the paralysis of the bowel, although it seemingly would be counterindicated. In cases where septic peritonitis is present at the time of operation, and there is danger of such peritonitis remaining as a postoperative complication, the Murphy **proctoclysis** is invaluable. This consists of the very slow instillation of warm saline solution into the rectum continuously for a long period of time, and many forms of special apparatus for the purpose have been devised. The apparatus of Dr. Robert C. Kemp maintains an even temperature of the saline solution by the use of the vacuum principle in the container of the fluid, similar to that obtained by the thermos bottle. The methods here described for treating cases with spreading peritonitis assume that we have made provision for sufficient drainage and have applied other resources in an operative way.

Poisoning by bichloride of mercury and by iodoform have in the past been common postoperative complications, although at the present time they do not occur so frequently, but still require attention. Poisoning by bichloride of mercury through absorption from large wound surfaces gives rise to the characteristic irritation of the mucosa of the alimentary tract, but seldom appears in abdominal work, because there is almost no situation in which an expert operator would think of using bichloride of mercury. Iodoform, however, is very frequently used in abdominal surgery, but chiefly with iodoform gauze, and this gives rise to iodoform poisoning so frequently that the author on one occasion, when being asked to look for it in a hospital ward, found several cases unsuspected in one ward. Iodoform is taken up very rapidly by the peritoneum, and its symptoms are commonly mistaken for the symptoms of septicemia, with rapid pulse, wet skin, and peculiar mental wandering.

Where we have occasion to suspect that iodoform poisoning is a postoperative complication in abdominal work, we may determine the point by adding a pinch of calomel to some of the patient's urine in a saucer, and stirring with a wooden spatula. If free iodine is present in the urine it makes the customary reaction to iodide of mercury, distinguished at once by the cloud of color. Removal of iodoform gauze from the wound in such a case, and taking up iodoform which is adherent to the tissues by pouring **sterilized oil** into the cavity from which the gauze was removed, and leaving the oil there for some minutes before abstracting it with absorbent apparatus, will commonly allow the patient to recover from a severe case of iodoform poisoning.

Patients vary greatly in their susceptibility to iodoform, and the author observed one death from iodoform poisoning with characteristic signs in a young girl, sixteen years of age, in a case in which he arrived too late in consultation. And the young

girl had been poisoned by a roll of iodoform gauze, not much larger than two fingers in size, after an appendix operation. The surgeon in charge had been absolutely at a loss to account for the symptoms. While there are positions in which iodoform gauze is of considerable value in small quantities in abdominal work, we must always bear in mind the danger of the postoperative complication of iodoform poisoning.

> In an attempt to discover the cause of the skin eruptions seen so often after abdominal operations, the author found that these occurred most often in patients who were given an enema of soapsuds made from common yellow soap, but if Castile soap were substituted no eruption followed. This was corroborated by the fact that in exchanging the yellow for the Castile soap in other patients who had these eruptions it was found that the yellow soap produced rashes, whereas the Castile soap did not. It was then found that the cheap and common yellow soap contained a considerable quantity of resin, and to this the writer believes the cause of many of the rashes seen after abdominal section must be attributed. F. J. Shepherd (Jour. of Cutaneous Dis., July, 1909).

Uncontrollable vomiting immediately following operation is probably due to excessive stimulation of the nerves of the stomach through shock, or from the irritation of ether which is being excreted by the glands of the stomach, and it seems to be due also at times to reversed peristalsis of the upper part of the bowel, throwing contents of the duodenum into the stomach, and the continuance of the wave of reversed peristalsis to the point of including the entire stomach. This complication sometimes becomes so dangerous that we must stop it by the chief means at our control, giving the patient the harmful **morphine.**

Properitoneal hernia is sometimes the cause for ileus with its vomiting and other train of symptoms, but it is not likely to occur in cases in which the operator is aware of the danger of this complication, and has guarded against it. Properitoneal hernia occurs in cases in which there has been defective suturing of the peritoneal layer of the abdominal wall after operation, and a small knuckle of bowel is forced by vomiting or cough into the space between the peritoneum and muscular abdominal wall.

Hernia into a rent in the omentum may occur as a postoperative complication, and, if, in the course of separating adhesions, the operator has left any small openings in the omentum, these should be extended clear to the margin of the omentum, or closed by suture. In any event, possibility of hernia complication should be foreseen in all work which deals with the omentum, if rents are left unclosed.

Perforation of the bowel sometimes occurs as a postoperative complication at the site where a rigid drainage tube or bulky drainage apparatus has caused an undue amount of pressure, and perforative ulcer may occur a few days after the operation at the site of a gastroenterostomy, if the bowel has been fastened so far away from the pylorus that acid contents of the stomach escape directly into the bowel at the point of juncture.

Postoperative phlebitis occurs often enough to require attention. It may appear two weeks after an aseptic operation, and its origin is not well understood. As a postoperative complication in appendicitis, it sometimes

appears as an inflammation of the left iliac vein or left saphenous vein, and occurs in fact at a distance quite as often as at the site of operation. While causing a high degree of discomfort and prolonging the period of illness, it is not often an absolutely dangerous complication. If abscesses are formed, they are apt to remain localized rather than to give rise to septic embolism.

Pylephlebitis does not often occur as a postoperative complication, excepting in cases in which we have evidences of its presence in advance of operation, but abscess of the liver may appear so late after an abdominal operation that the relationship between the primary focus of infection in the peritonal cavity and the liver abscess may be lost sight of. A patient may even leave the hospital, and his home, and travel to a distance for recuperation, with beginning abscess of the liver, the treatment for which will receive consideration under the heading of that subject.

Secondary abscess may appear at the site of an infection which has been cared for at the time of operation, but such secondary abscess is prone to liquefy newly coagulated lymph toward the external abdominal incision, and to follow this line of least resistance, rather than to extend in other directions.

Mesenteric thrombosis not markedly present at the time of an operation may increase to become a postoperative menace, due probably to injury of the veins in the course of an operation, but the complication is rare.

Bladder complications do not call for special consideration in this article. The bladder sometimes refuses to contract in a normal way after various abdominal operations. This is sometimes due to nothing more serious than the unaccustomed recumbent position of the patient, or to physic influence, although shock sometimes leads to disturbance of the innervation of the bladder, and at the same time we are apt to have hyposecretion of urine due to a similar influence upon the kidneys. It is best to avoid using a catheter if possible for emptying the bladder, and it is seldom necessary, excepting when we have direct evidence of an overfull bladder. Otherwise it is best to resort to such resources as massage of the bladder above the pubes, and the sound of trickling water upon a warm bedpan placed beneath the patient. If we begin too early to use the catheter, there is a tendency for the bladder to depend upon that resource for some days, and sometimes for as long as the patient remains in bed, if we begin with the mistaken idea that prompt use of the catheter will simplify matters.

Postoperative psychoses occasionally occur after abdominal operations, and the operation is commonly held by relatives of the patient to be the primary cause. Such disturbances usually mean the precipitation of impending psychoses which were developing in advance of the operation, but kept in check by the will of the patient until the shock and surroundings of the operation relaxed that control. Such psychoses may be due to central causes, but are also sometimes toxic in origin, as the abdominal surgeon sees them, and such psychoses precipitated by operation may be really on the road to elimination, due to removal of the origin of the toxic impression.

Peritoneal adhesions causing trouble subsequent to operation receive consideration along with that general subject elsewhere in the article.

Postoperative pneumonia occurs, according to various authors who have tabulated many thousands of cases, in from 2 to 5 per cent. of all abdominal operations, although in practice one may have series of one or two hundred operations without a single case of pneumonia, and it is very much less frequent today as the result of our refinement in technique than it was ten years ago. True croupous or lobar pneumonia, lobular pneumonia and hypostatic pneumonia may all stand in direct relationship to causes which are more or less under control by the surgeon. The development of true lobar pneumonia, developing immediately after an operation, seems to the author to be more than a coincidence. The disturbance incident to any abdominal operation may lower the vitality of the patient in such a way that the omnipresent pneumococcus may suddenly spring into activity, particularly if ether has been the anesthetic. We have recent knowledge that infections of various sorts may begin quickly in animals under the influence of that anesthetic. The shorter the period of anesthesia, and of operative procedure which lessens general resistance, the less we shall probably have of true lobar pneumonia, which has generally been held to be merely coincidental.

Hypostatic pneumonia after abdominal operations may appear for the same reasons that it appears elsewhere, but neither hypostatic nor true lobar pneumonia are so distinctly traced as postoperative complications as is lobular pneumonia, and this lobular pneumonia is the particular one with which we usually have to deal. According to statistics, lobular pneumonia occurs more often after abdominal operations on the aged, and more often in men than in women, but the latter feature of the statistics does not have special reference to abdominal operations. While general anesthetics are all more or less irritating to the bronchial mucosa, and postoperative vomiting is a factor allowing aspiration of mucus or substances from the stomach, there are other features leading to a special preponderance of lobular pneumonia after laparotomy. The pain following abdominal operations interferes with full range of the muscles of respiration and favors pulmonary stasis, but direct infection of the lungs by bacteria may occur in three ways: by way of the mucous membrane, the blood- and lymph-vessels. After abdominal operations, with a tendency to pulmonary stasis because of limited respiration on account of abdominal pain, and retention of matters which would be expectorated if coughing were not so painful, bacteria arriving at the lungs from the abdominal region by way of the blood- and lymph- vessels meet with resistance which is less than normal. The author believes that long exposure of the peritoneum in the course of an ordinary operation may lead to the carrying of large numbers of air bacteria indirectly to the lungs without complete destruction *en route* by phagocytes, and it is his impression that these cases are not infrequent. Embolic pneumonia and its common sequence of lung abscess by infection through the

blood-stream no doubt occurs from the handling of thrombosed vessels, and, while we recognize certain cases of pneumonia directly due to the presence of the larger emboli, it is probable that we have many other cases in which minute emboli give rise to complications which appear a few days after operation.

Pleurisy frequently follows operations upon the liver and gall-bladder, if these operations are for cases with infection. Here it is probable that infection is transmitted by way of the lymphatics through the diaphragm to the pleura, and the neighboring lung becomes next infected, giving us sometimes the dangerous pleural pneumonia. The postoperative complication of pleurisy or of pleural pneumonia cannot well be guarded against, but we may anticipate the danger of postoperative lobular pneumonia, and lessen this complication very distinctly in several ways: by avoiding as far as possible unnecessarily prolonged operations with the accompanying long period of anesthesia; by maintaining the body warmth of the patient, and by allowing the patient postures which favor expectoration. It is probable that the Fowler position after operation, while not particularly favoring expectoration, may lessen the danger from embolic pneumonia to some extent.

Fistulæ from the alimentary tract and bile-tract are sometimes annoying as postoperative complications, but when not formed purposely for useful purposes they have a remarkable tendency to close spontaneously if left alone. Very much harm is done almost as a matter of routine at the present moment by surgeons, house staff assistants and nurses in their efforts at keeping such fistulæ carefully cleansed. Antiseptics introduced into such fistulæ cause disturbance of the delicate new cells which are being thrown out for purposes of repair, and even so harmless a solution as saline solution is commonly injurious in fistulæ. Employment of hydrogen dioxide, which cleanses fistulæ in a most attractive way, is one of the most injurious of resources, because it destroys new cells quite as readily as it destroys pus. In cases in which we have reason to suspect that a fistula is kept open by something at the bottom of the fistula, as a knot of unabsorbed ligature, a concretion, a bit of fecal matter, or other foreign body, we shall usually need to operate, for efforts at closing such fistulæ are usually very futile until the foreign body is out.

Excepting in cases in which we believe that a foreign body lies at the bottom of the fistula, our treatment had best be a treatment of neglect, doing nothing whatsoever in the way of cleansing the fistula, and simply using an external dressing for the purpose of cleanliness. Under this treatment new repair cells quickly form connective tissue, and such connective tissue, according to its well-known habit, contracts regularly and closes fistulæ. There are a few cases in which epithelium will move downward from the skin and upward from the bowel, forming an epithelial covering for the walls of a short fistula, and when such short fistulæ are seen to have an epithelial lining this may be destroyed by leaving 95 per cent. carbolic acid along the line of the fistula for half a minute, and then neutralizing it with alcohol. After

the destruction of epithelium in this way by carbolic acid, new cells are formed, but we must be sure that epithelial cells do not again cover the surface, and to guard against this the highly astringent subsulphate of iron is effective as an astringent which will not allow new epithelial cells to grow, but which does not prevent the development of connective-tissue cells, although connective tissue formation in such cases is tedious.

One of the most persistent fistulæ in the author's practice followed an operation for perforating ulcer of the duodenum, in a patient whose large size and desperate condition did not allow detailed work at the ulcer site at the time of operation. This fistula discharged pancreatic secretion, bile and chyme for some months, but finally closed spontaneously. As a rule, it is best to allow the patient with a postoperative fistula to get out of bed as soon as the wound is secured in the ordinary way, and the patient then goes about his ordinary occupation and engages in all sorts of activities, with no attention to the fistula beyond the wearing of a small external pad of gauze for the purpose of neatness.

Objects left behind after abdominal operations have led to complications in imposing array among statistics, and the gauze pad has been the chief offender.

> Reports of 100 cases of foreign bodies left in the abdomen after celiotomy. Fifty-eight patients recovered; 42 died. Twenty-nine times a sponge was lost, twenty-eight times a tampon or gauze compress, four times a drainage-tube, and nineteen times artery forceps. In a number of instances two foreign bodies were left in. The sponges were generally recovered by second section. The majority of tampons and compresses were discharged spontaneously through the rectum. Neugebauer (Zentralbl. für Chir., Nu. 3, 1900).
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> The writer has collected 155 cases in which foreign bodies were left in the abdominal cavity, suggesting how frequent this serious accident is. The foreign body may cause an acute or a low and protracted form of sepsis; be encapsulated and retained for months or years; or be extruded through the wound, or into the hollow viscera; or, more rarely, through the cicatrix. The accident has occurred despite repeated counts of sponges, and the plan of attaching tapes to the sponges is shown to be fallible. In a number of instances a sponge was torn in two during the operation. It is advised that abdominal operation be done with the simplest equipment practicable. The responsibility rests with the nurse or assistant charged with the enumeration of the sponges and instruments, not the operator. Schachner (Annals of Surg., Nov., 1901).
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> In 1899 the writer found records of 108 cases, and in 1904 he had collected 88 more—a total of 236 cases, not to mention a number of others in which the correct details are not known. Neugebauer (Archiv für Gynäk., Bd. lxxxii, F. v. Winckel Nu., 1907).

When one or more objects have been left behind in the peritoneal cavity the patient may go on to recovery, but usually there is a persistent nausea and a higher degree of local tenderness and discomfort than we can usually account for, and the persistence of such condition of nausea and distress at the site of an operation may lead one to feel that it is best to reopen the abdominal cavity and search for a foreign body which has been left behind. This postoperative complication is not so easily guarded against as one might imagine; but gauze for intra-abdominal work, to which tapes have been attached in the form of a long roll, one end of

which is always left outside of the abdomen to guard against accident, should be employed.

Case in which, after removing a piece of gauze which had remained in the cavity for two months, the writer was obliged to resect the intestine in three places, the patient eventually making a perfect recovery. He reports 17 cases in which gauze was left after operation, only one of which terminated fatally. In 9 the foreign body was discharged spontaneously, in 8 removed by operation, but in none were such extensive lesions found as in the case reported. Kayser (Archiv für Gynäk., Bd. lxviii, Hft. 2, 1903).

Case of simulated ovarian tumor which proved on operation to be a completely encysted compress, relic of some former surgical intervention. Experiments on animals confirmed the possibility that an overlooked sterile compress can be thus encysted, and also, further, that such a compress may work its way through into the gut and be spontaneously evacuated. He has found 41 cases on record of a compress having been left in the abdomen. In 9 the patients died soon after, with symptoms of peritonitis. Riese (Archiv für klin. Chir., Bd. lxxiii, Nu. 4, 1904).

Case of an old woman who had retained a long Terrier compression forceps (22 cm. long) in her peritoneal cavity for seven years. She complained of pains in the abdomen and noted a projecting point of some sort at the lower part of the abdominal wall. The forceps could be felt in Douglas's space by rectal examination, and it was removed through a posterior vaginal incision. The patient made a good recovery. Grousdieff (Roussky Vratch, July 29, 1906).

The writer attaches each compress or piece of gauze, used after the abdomen is opened, to the wire basket in which they were sterilized. Only large compresses of several layers of gauze are used, and to each compress is attached a piece of narrow tape over six feet long. The free ends of the tapes are passed through the meshes of the wire basket and tied together. The basket may be placed on the floor under the table. The tapes are not annoying after one is used to them. Wechsberg (Zentralbl. für Gynäk., Nu. 12, 1907).

Case in which a patient apparently secreted portions of gauze in her vagina after an abdominal operation, with the view of misleading her family attendant into the belief that they had been left in the abdomen after operation and were escaping through a fistulous opening. The writer uncovered the trick, and reports the case as possibly throwing a sidelight on the subject of some alleged cases of foreign bodies in the abdomen, and as a source of blackmail. M. F. Porter (Jour. Indiana State Med. Assoc., April, 1908).

Secondary hemorrhage as a postoperative complication occurs more often in abdominal surgery than elsewhere, because of violent vomiting, which dislodges sutures and ligatures. This must always be borne in mind, and we avoid the accident by introducing as few mass ligatures as possible, and ligating vessels separately. Very many cases of secondary hemorrhage have occurred after ligation of the broad mesentery of the appendix, or of a broad ligament, because contraction of the psoas and iliac muscles, in addition to the other muscular contractions in vomiting, has a tendency to broaden out the peritoneal base and force off such ligatures, unless they have been tied with caution. Secondary hemorrhage occurs also when violent vomiting has caused fine sutures of silk or thread to cut out under tension, and for this reason the author favors sutures of larger caliber than are commonly employed. Where large vessels have been opened, and secondary hemorrhage occurs marked by the ordinary signs of increasing thirst, restlessness,

pallor, pain and rapid pulse, we must reopen the abdominal cavity for securing bleeding points and removing blood, and this is usually a very dangerous procedure because of the condition of the patient, requiring preparation for direct infusion of blood or introduction of intravenous saline solution at the moment the abdomen is reopened. Another form of secondary hemorrhage occurring after operation is common when the force of the arterial pulse is sufficient to give *vis a tergo* to blood in veins torn in separating adhesions, and which are not bleeding much at the time when the operation is completed.

Since von Eiselberg published his first observation on gastric and intestinal hemorrhages following operations (1899) many other authors have written on the subject. Most of them are in accord with von Eiselberg's theory of the causation of these hemorrhages; namely, that they result from thrombotic and embolic processes in the territory of the gastrointestinal circulation.

The author has studied 30 cases of gastric and intestinal hemorrhages after operation. All these cases were operated upon for acute or chronic abdominal conditions; 17 patients died after the operative procedures. At the post-mortem examinations, in most of the cases, very little could be found to account for the ofttimes profuse bleeding during life. It may in general be stated, however, that the anatomical alterations consist in hemorrhages into the mucous membrane, hemorrhagic erosions, or small ulcers. These lesions are to be found in the stomach or duodenum; the remainder of the intestinal tract is usually negative. These anatomical changes result from injury to the corresponding blood-vessels. Such injury may be: 1. Blocking of the veins from retrograde emboli or from a progressing venous thrombosis. 2. Paralysis of the circulation in localized areas, the effect of the circulating poison or, in rare cases, the result of an affection of the central nervous system.

The gastrointestinal hemorrhages occur most frequently in the first three days after operation. When the condition from which the patient is suffering is not fatal the gastric or intestinal lesions rapidly get well; the lesions are thus not true ulcers. The prognosis in individuals suffering from profuse hemorrhages is, in the presence of a general infection, very poor. J. R. von Winniwarter (Archiv f. klin., Bd. xcv, Theil 1, 1911; Amer. Jour. of Surg., Sept., 1911).

After any aseptic abdominal operation considerable blood may escape into the peritoneal cavity without causing a great degree of disturbance beyond the increase in local pain, which is the characteristic sign of such hemorrhage. Aseptic blood in the peritoneal cavity is still in the circulation in a way, because the peritoneal cavity is a lymph-chamber, and the serous remains of the blood which escape in the course of coagulation are taken up into the blood circulation again. **Morphine** lessens the hemorrhage and strychnine increases it. Bearing these facts in mind, we may sometimes give the dangerous morphine to advantage, or withhold the strychnine unless it is greatly required.

The writer reports 5 cases of collapse of the lungs after abdominal operations. The symptoms are sudden dyspnea and cyanosis, with, perhaps, pain in the lower part of the chest and a slight cough. On the same side as the operation there is dullness at the base, with weakness of the breath sounds, which ultimately become inaudible. The movements on the healthy side, on the other hand, are exaggerated, and the lung apparently becomes enlarged through a process of compensation. Pasteur (London Lancet, Oct. 8, 1910).

TOILET OF THE PERITONEUM.—The peritoneum protects itself so well, if given opportunity, that we need pay very little attention to securing asepsis of any part of the abdominal cavity while we are at work. If pus escapes upon normal peritoneum when abscesses are opened, it commonly causes no harm, even though it be left upon the peritoneum when we are through with the operation. There are two reasons for this. Bacteria are chiefly at work in the tissues rather than in the pus proper, and the latter is often practically sterile, even in the presence of advancing infection. By pus I do not mean intraperitoneal fluids teeming with bacteria, but these are for the most part not walled in like pus. The principle, however, of treatment is practically the same; for where such fluids occur any special effort at securing asepsis would be futile, and, more than that, likely to be harmful.

We may quickly arrange drainage for such septic fluids, but efforts at wiping or washing them out are apt to lead to injury of the endothelial covering of the peritoneum, and to defeat the object of our good intentions.

When fluids carrying bacteria or sterile pus in quantity should be removed, it is best to do it very gently by quick absorption into masses of absorbent gauze, rather than by sponging or flushing, and we take good care at the same time to avoid the wiping which injures endothelium. Where stomach or bowel contents are likely to escape in the course of an operation, it is well to protect the field with absorbent gauze, but such gauze adheres quickly and firmly to normal peritoneum, with injury to its endothelium. Where we can apply the resource of placing a layer of rubber dam between peritoneum and gauze while we are at work, we guard the peritoneum in the best way. The peritoneum, while protecting itself remarkably against infective material, is disabled by the washing and wiping commonly employed, and particularly by the application of germicides, almost any one of which in the peritoneal cavity is productive of damage.

A peritoneum which would be perfectly safe, even though considerable septic fluid were left upon it, may when disabled start out on a career of infection which would have been avoided if we had not tried in a crude way to make the peritoneum ideally clean. In the vicinity of the focus of infection within the peritoneal cavity a local hyperleucocytosis becomes established with extreme rapidity, and this does away with the necessity for much of the work in toilet of the peritoneum described by authors in general.

There are occasions in which it is desirable to evacuate very large quantities of pus or septic fluids quickly, and for this purpose **hydrogen dioxide** may be used, provided that all exits are kept free, and that the only peritoneum with which it comes in contact is peritoneum already damaged. Hydrogen dioxide damages normal peritoneum instantaneously, and is to be used only where the peritoneum has already suffered great damage, but in such situations it throws out pus and septic fluids in a great foaming mass, and, this mass removed, **saline solution** may follow, leaving the cavity very clean.

While **hydrogen dioxide** is germicidal, its value rests in its mechanical effect in throwing out albuminous fluids and débris rapidly, rather than in securing asepsis where it is not needed, and when efforts to secure it through the use of germicides are damaging. For most cleansing purposes in the peritoneal cavity **physiologic salt solution** is the best, although even that is to be used with caution. If it is not employed with too much force or removed too vigorously it has a field of value. The solution of nine-tenths of 1 per cent., isotonic for human blood-serum, is more benign than the commonly employed six-tenths of 1 per cent. which is isotonic for frogs' blood, and which had its origin in the laboratories. The saline solution should be sterilized by boiling.

Sterile water, even though boiled, should never be used within the peritoneal cavity unless it contains salt. The reason why water without salt should not be used is because it is corrosive. Its corrosive nature may be noted at once by dropping it in the eye, which leads to immediate smarting and burning of the conjunctiva. Water without salt is so destructive to delicate tissues in laboratory work, and the fact is so well known, that it is a strange omission on the part of many authors to neglect to state the dangerous character of water without salt.

The reason why even sterile pure water is corrosive is because an osmosis of salts from the body cells immediately occurs in the presence of water not containing those salts in the proportion in which they are found in the body cells. Chloride of sodium, however, being the chief salt involved, is the only one which we need to add to the water for practical purposes in routine work.

Dawbarn poured milk representing septic fluid into the peritoneal cavity of a cadaver, and then set to work to find the best way to get all of the milk out again, and after a very great deal of flushing and sponging found that some milk still remained.

This showed how impossible it is to remove the septic fluid by any mechanical toilet of the peritoneum, and demonstrates the degree of damage to peritoneum which will occur incidentally through our efforts. Consequently the toilet of the peritoneum is best left in part to the peritoneum itself, aided by such resources as we have learned do not cause damage. As the result of experimentation some authors have closed the peritoneal cavity completely without drainage in cases in which it was known that some septic areas remained behind, depending upon the peritoneum to dispose of any sepsis after the chief focus of infection had been removed. While primary union often occurs in such cases, the author believes that at the present time it is best to use small capillary drainage apparatus for removing culture fluids from the septic site.

DRAINAGE OF THE PERITONEAL CAVITY.—Because of atmospheric pressure upon the abdominal contents, any free fluid within the peritoneal cavity has a tendency to follow the line of least resistance to the surface, and if this fluid is given direction by way of small capillary drains we fulfill the general indications in drainage, but posture of the patient is an aid under some cir-

cumstances; and the Fowler position, in which the upper part of the body is raised in bed to an angle which will allow fluids to gravitate to the drain in the lower part of the abdomen, is at times very useful. The only objection to the Fowler position is the call for rather more work on the part of the heart in a very weak patient.

In the upper part of the abdomen we have a natural mechanical situation, aiding drainage from the bile-tract region, in what is known as Morison's pouch, the space between the liver, above, and the stomach and colon, below. Blood, bile or septic fluids escaping into this pouch have a tendency to make their way directly to the surface at this point, instead of spreading into the general peritoneal cavity below, and this tendency is so marked that a very little capillary drainage carried to the bile-tract region suffices to clear the area of culture media. It even allows us to do away with suturing the common bile-duct in many cases in which this has been opened for removing a calculus.

Abdominal drainage is well conducted by any of the means described under the head of drainage apparatus, and the author feels that it is always best to employ capillary drainage, rather than drainage through tubes which carry no gauze wick. When a tube without gauze wick is filled with fluid, the column of fluid in the tube exerts hydrostatic pressure of considerable degree, which is met by the atmospheric pressure of the viscera, to be sure, but drainage through a simple tube cannot be so free as when fluids are guided through the tube by absorbent gauze with its high degree of capillary power. Drainage apparatus should be carried as little as possible among intestinal loops, because such drainage apparently acts as a foreign body, and the peritoneum rapidly throwing out lymph because of the offense seals in such drainage apparatus and deprives it quickly of its usefulness.

If the abdominal work carries us to the pelvis, there is sometimes an inclination for the surgeon to add vaginal drainage, because the Douglas pouch represents the lowest part of the abdominal cavity, and one would naturally feel that fluids would all gravitate to this lowest point. This is not quite true, however, in practice, as atmospheric pressure has a tendency to force even pelvic fluids to the midline incision in the abdomen, with or without encouragement from capillary drains, and the advantage of depending upon drainage through an abdominal incision rather than through a vaginal incision depends upon the comparative ease with which the area of the abdominal incision is kept aseptic. Drainage in the vaginal region is in an area much more difficult of maintaining in a degree of relative asepsis.

The author formerly felt that it was an advantage to insert drainage apparatus at more than one point in the abdominal wall at points that seemed natural places for collection of peritoneal fluid, but of late years, in a series of many hundreds of abdominal operations sufficient to demonstrate the real requirements, he has found that one point for drainage in the lower abdomen will suffice, and the only additional point used for drainage for many years has been in reference to Morison's pouch, which

amounts practically to a separate cavity more distinct than the cavity of the pelvis so far as the question of the necessity for drainage devices is concerned. We need to give aid to a single incision drainage at times by the addition of posture.

In order to carry out the principles of capillary drainage it is essential for one to be familiar with the mechanical principles involved, and to make frequent change of the external mass of gauze to keep the capillary drain at work within the abdomen. In cases in which fluids drained from the peritoneal cavity are irritating to the skin, the skin may be dried temporarily, and then covered in the vicinity with a thin layer of collodion or of vaselin. In addition to the drain for the peritoneal cavity, it is important, on closing the abdominal incision, to leave a tiny wick drain for twenty-four hours, extending between the muscle layer and the skin. This can rest between the sutures in such a way as to interfere not at all with final primary union. At the end of twenty-four hours, or at the time of the first dressing, it may be pulled out, and will be found to have drained out as a rule quite a little serum or free fat, or both, which would have been a menace as a culture medium. Excepting in patients with a very thin adipose layer, it is well to make it a rule to introduce this tiny drain at any convenient point between the sutures, and to remove it on the following day.

HEMOSTASIS.—A few technical points belong to hemostasis in abdominal surgery. Where it is possible to use torsion instead of ligatures—and this covers very much of the field—we can avoid ligatures, the presence of which causes the peritoneum to throw out plastic lymph in the vicinity for its protection, very much as the mollusk throws a layer of nacre over a grain of sand in the shell. Where it is necessary to use ligatures we avoid including much mass in the ligature, because, the larger the mass, the greater the tendency for the peritoneum to throw out reparative lymph which will lead to adhesion formation subsequently. We have also to remember that the efforts of vomiting after an abdominal operation have a tendency to pull off certain ligatures, and consequently we must leave a considerable mass of tissue outside of the knot. Such mass of tissue is not likely to slough, as some operators fear, because it is kept alive by lymph circulation in the vicinity, and has a tendency to gradually become absorbed in a very benign way, because of the fact that it is tissue belonging to the individual. Hemostasis of the cut margins of the alimentary tract cannot readily be obtained by ligating, and consequently we employ the suture here instead, for the most part, and snugly drawn running sutures suffice for the purpose.

EXTERNAL INCISIONS.—The ultimate success of an abdominal operation often depends largely upon the choice of the external incision, and we have two especial points to bear in mind: consideration of the best route for getting to any objective point within the abdominal cavity, and at the same time the best way for avoiding imperfect repair of the abdominal wall and unsightly scars.

This includes a consideration of avoiding nerves which supply muscles, because a temporary or perma-

nent paralysis of certain abdominal muscles was a very annoying post-operative complication before surgeons began to give attention to this matter. To reach an objective point in the peritoneal cavity, and at the same time avoid the complication due to muscles cut transversely, we may practically cover the ground by stating that it is well to plan to make separate division of each layer—skin, adipose tissue, fascia, muscle and parietal peritoneum—and, further, to make blunt dissection as far as possible of each muscle, even though this sometimes leads to openings crossing each other at somewhat different angles. Stretching of the muscle wound with the fingers, however, does away with most of the awkwardness of a situation where split muscles, after blunt dissection, as it is called, lie at different angles.

When, for any reason, it becomes necessary to cut transversely across a muscle we must mark well the point at which such transverse incision was made for the purpose of making accurate repair subsequently, otherwise the muscles acting in their lines of traction during the course of the operation will smooth out angles more by transverse incisions, and it is difficult to restore these angles again. On general principles our incisions are to be made directly over the objective point, but because of the ease with which an incision is made into the abdominal cavity in the median line, and the ease with which such an incision is repaired, the mid-line incision should be used for perhaps the larger part of our abdominal work.

The size of incisions will depend largely upon the operator. One must make as large an incision as he needs for working freely and safely, but, if experience allows an operator to make his incisions shorter and shorter safely in any particular field of abdominal work, the patient will have the advantage of less danger from subsequent hernia, less shock, and less noticeable scars. Small incisions are dangerous for the beginner, and plenty of room is desirable on his account, but he may adopt the middle ground of beginning with a comparatively small incision, and then enlarging it as occasion requires.

If the abdomen requires opening in two different localities at the same sitting, there is frequently an advantage in making two or more small separate openings, rather than extending a large one to reach distant points, such as often occurs in cases of intestinal obstruction, where one is not sure of the point of the obstruction. If through the first incision, in a case of obstruction, one does not readily reach the point at which the constriction occurs, he is likely to add much more to the serious condition of the patient if he makes a large incision and pulls the bowel out from that than he is if he makes more than one incision small, and then passes the bowel between his fingers at that point without drawing it out upon the abdominal wall. Special incisions will be noted in connection with certain operations, the above covering only a general principle.

When we have occasion to open the abdomen at the site of a former operation, it is well to carry the incision through normal skin on either side of the scar line for two reasons: because of the advantage of removing the scar tissue in some cases, and

because in opening at the site of an old scar one may run across adhesions of abdominal viscera of which he was not aware, and they may be injured. The safe way for entering along the site of an old scar, and for leaving the viscera in good condition for repair subsequently, is to go down through normal tissue on either side of the scar until muscle sheath is definitely reached, and then snipping muscle sheath until the muscle beneath is seen. The sheath can then be opened freely on either side of the scar without danger. If there is any question about adhesions being present at just this point of dangerous character, we extend the incision through the sheath of muscle to some point above or below the scar, where we may enter the peritoneal cavity at a point free from adhesions, being extended at a free point large enough to admit the finger. The finger is then carried back along the peritoneal side of the scar line, and adhesions if present are separated. This having been done, the posterior sheath of the muscle and transversalis fascia and peritoneum are safely cut along the entire line of the scar, and the parts left in excellent position for correct apposition subsequently.

One must always be on guard against small hernial protrusions into scar sites, and a small knuckle of bowel may be adherent in such protrusions without having led to symptoms sufficient for one to suspect its presence. Ordinarily, on reaching the peritoneum or subperitoneal fat, it is not necessary to pick it up and divide between forceps, if one has reason to believe that no adhesions occur at that point. Under ordinary circumstances, the various layers of the abdominal wall having been opened down to the peritoneum, or peritoneal or subperitoneal fat, these structures may be made tense between two fingers of one hand, and the points of scissors then introduced into this tense area nearly parallel with the plane of the abdominal wall, a neat entrance into the peritoneal cavity is made with celerity. This opening can then be enlarged to any desired extent with the scissors, or in many cases by stretching.

Closure of the abdominal incision may also be described in a general way to cover most of the principles involved. The first suture of the peritoneal incision should consist of the finest catgut, because, the smaller the strand of catgut, the less peritoneal irritation from the suture, and consequently less tendency to adhesions of the omentum which reaches out to wall-in points of irritation within its range. A fine strand of catgut is also a distinct advantage along the line that would be touched by the liver, which slides along the abdominal wall with each respiratory movement.

> Suturing the incision in the abdominal wall in layers gives a more satisfactory and stronger looking wound histologically than the *en masse* suture. Wounds sutured in layers were the stronger after two weeks, the strength of the scar having been tested by an actual pull. Judged from a histologic study, the suture in layers is also more desirable than the suture *en masse* because in this way in the process of repair the strong trabecular tissue arising by proliferation from the fascia united with tissue of its own kind, thereby increasing the strength of the scar and decreasing the time necessary for repair.
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> Violent manipulations of the edges of an abdominal incision should be avoided with the same care as has been recog-

nized as essential to good results in the handling of the intestines or stomach. Murphy (Boston Med. and Surg. Jour., March 7, 1907).

In experimental work with animals in the course of which the author closed peritoneal incisions with rather large strands of catgut or silk for the purpose of saving time, he observed that adhesions of intraperitoneal structures of some sort along the suture line are practically universal. He observed that the smaller the strand of catgut, the less postoperative adhesions occurred, and although such adhesions commonly become absorbed they remain just often enough in practical surgery to make it a very general point to avoid them as much as we can. Very little strength indeed is required for approximating peritoneal margins, and a suture which would be absorbed in forty-eight hours is all that is required, and a very small strand at that.

In the closure of an abdominal incision the writer overlaps the cut edges of the rectus fascia. The peritoneum is sutured with catgut, and the same suture is used to whip together the muscle. On the right side of the wound the fascia is separated back from the muscle for from 1 to 3 cm.; likewise on the left side. Tension sutures are then introduced through the skin about 3 cm. from the edge of the wound, passing through the fat and the fascia about 1 cm. from the edge, then in and out through the fascia on the left side from 1 cm. to 3 cm. from the edge, and back through the fascia on the right side, then out through the fat and skin on the left side. The sutures are placed from 4 to 5 cm. apart. Next the edge of the overlapping fascia is whipped down with chromic catgut, and the skin sutures with a buttonhole stitch. If the ends of the tension sutures are drawn taut, the fascia will overlap, and the whipping down of the edge will be facilitated. Gauze saturated with 70 per cent. alcohol is placed over the wound, and the tension sutures are tied over the gauze. The tension sutures are removed in from ten to fourteen days.

Lucas-Championnière conceived the idea of overlapping the fascia in the operation for inguinal hernia, and employed the method as early as or even earlier than 1892. To Dr. Charles P. Noble is due the credit of being the first to use, describe, and make popular the method in America. He began to overlap the fascia in 1894 and used it as a routine procedure in the closure of all abdominal incisions after 1896. The method of Lucas-Championnière is now used with many slight modifications in technique by surgeons all over the country. S. E. Tracy (Surg., Gynec., and Obstet., April and Sept., 1911).

It is the sheaths of the muscles upon which we depend for strength when closing an abdominal incision. Suturing of the sheaths of the muscles is carried out neatly by using a continuous suture of chromic gut along the posterior sheath first, and then returning along the anterior sheath without introducing sutures into the muscle itself at all when the incision is made in the median line of the abdomen, and the same principle can be used in several parts of the abdominal wall. Muscle belly does not hold sutures so well as muscle sheaths, and there are few situations where it is necessary to introduce sutures into the muscle belly. By bringing the posterior and anterior sheaths of muscles into their respective normal positions, atmospheric pressure carries the bellies together much more evenly than we could do it with sutures.

Several fanciful methods for suturing the various structures of the abdominal wall have been described,

but it is not necessary to do anything more than to leave structures as we found them as nearly as possible. Where one can catch the transversalis fascia along with the posterior sheath of a muscle in a suture, it is well to do so.

In cases in which there may be need for reopening the abdomen subsequently, interrupted sutures of the muscle sheath for a part or all of the way are of advantage, because then we reopen only to the extent necessary. Where a drain has been left in an incision, the suture running up to the drain may be followed by a provisional interrupted suture, if it is desired to close the incision completely when the drain is removed, but this is seldom necessary, for proper suturing up to the small drains which are now in vogue will allow of the walls falling together naturally enough when the drain is removed.

One disadvantage of carrying the sutures through muscle tissue is the danger of the sutures cutting through such tissue when the patient vomits. This space then fills with blood which must be replaced by new tissue cells, and it usually is so replaced if the blood, as a culture medium, does not become exposed to infection from the suture, or some other source. For the muscle-fascia suture, chromic catgut, or kangaroo tendon is desirable, because they last so much longer than simply prepared catgut, but not so long as to constitute a source of irritation, as a rule. Kangaroo tendon seems to be much more benign than chromic catgut, and it lasts rather longer in the tissues, unless the catgut has been chromicized in a way which makes it too hard.

Where one needs to introduce interrupted tension sutures, there is nothing better than kangaroo tendon passed through muscle sheath, carefully avoiding the fat, into which no tension suture should ever be introduced. When closing the adipose layer of the abdominal wall, it is extremely important to avoid allowing any sort of suture to enter any fatty structure. The reason for this is because the entrance of any suture, or even the needle carrying the suture, into the adipose layer allows free oil to escape and to follow the course of the needle or suture, and such free oil, according to the principle of hydrostatics, will begin to travel, opening up lines for infection in many cases.

Where a very small amount of oil is set free along suture lines it is no doubt absorbed in many cases, but nevertheless always introduces a danger which is unnecessary, because we can apply a principle in mechanics commonly overlooked which allows us to do away with any suturing through any adipose layer of the abdominal wall. This principle is the one which is employed by the boy who lifts stones after pressing down upon them a disk of wet leather to which a string is attached in the middle. It is the principle of making use of atmospheric pressure. When the suturing of muscle sheath has been completed, if the adipose layers of the abdominal wall are then pressed together with the hands, they adhere firmly under atmospheric pressure the moment that the skin is sutured. It is somewhat difficult at the end of forty-eight hours to separate fatty tissues along the original line, if one has occasion for any reason

to re-enter the abdominal cavity. The question of suturing the adipose layer then may be disposed of by saying simply, *Do not suture adipose tissue at all.*

To overcome in most instances the difficulties of intra-abdominal operation in stout patients, the writer resorts to a large excision of skin and fat from the overweighted abdominal wall, removing a skin section either in the transverse or in a vertical direction corresponding to or at right angles with the incision, about 8 or 10 inches in length by 3 or 4 inches in width. This does away with the thickness of the wall down to the fascia, while from the fascia inward the difference between different abdomens is not great. If the patient is excessively fat, one will then naturally do a regular lipectomy operation. This serves the same purpose and is done the same as the lesser procedure here described. The writer emphasizes the value of removing wedges of skin and fat in patients who are not troubled with obesity, but simply and solely for getting rid of a part of the thickness of the abdominal wall and making the field of the operation more accessible.

An oval or an elliptical excision is made, cutting right down to the strong fascia overlying the rectus and oblique muscles. All bleeding vessels ought to be carefully tied. It is a good plan to slope the edges of the incision a little inward. When this piece of skin and fat is removed the operator then finds it much easier to open the abdominal wall and operate than in a similar case in which he has to retract this embarrassing mass of tissue as well. The writer closes such a wound with a fine catgut suture, catching a distinct layer of fascia about the middle of the fat, silkworm-gut sutures uniting both skin and adipose tissue. Kelly (Annals of Surg., March, 1911).

In suturing the skin the use of the subcuticular suture avoids scarring with a needle, and it also avoids the danger of making stab cultures of the *Staphylococcus albus,* which is found regularly as an inhabitant of the hair-follicles of the skin. Where very heavy abdominal walls are to be supported, we may fortify the skin sutures by placing squares of zinc oxide plaster at a short distance from the line of incision on either side of the incision, and then lacing these squares together through eyelet holes placed in the margins.

To avoid infecting the wound with the lacing, a thin layer of dressing is first placed next the wound, and then the squares of adhesive plaster laced together over this. We thus avoid altogether the necessity for introduction of deep through-and-through sutures, which in the past have been commonly used for supporting overheavy abdominal walls.

To avoid unsightly scars of the skin due to stretching out and widening of the scar line after union is complete, we put a single layer of gauze or chenille over the line of incision, and then pour on collodion. This collodion-gauze dressing may remain in place for two or three weeks if one wishes, and it constitutes a very neat resource for avoiding scarring of the abdominal wall for people who have a perfectly legitimate vanity in the matter.

The Pfannenstiel incision for laparotomy is commended by the writer, who employed it in 150 cases, 36 of which were cases of carcinoma operated by Wertheim's method (removal of the iliac glands). It is easy, the liability to hernia is decidedly diminished, the mortality is probably less than that of the median incision, and the only contraindications are those in which the vaginal route can be used, large fibroids, and cases in which there are many adhesions. Vertes (Zentralbl. für Gynäk., Sept. 24, 1904).

Pfannenstiel's incision may be used with good results in the Wertheim operation and for the removal of ovarian tumors if the cyst is punctured. It is not suitable in suppurative or tuberculous cases. It is believed to have important advantages over the median incision in many cases. Helsted (Zentralbl. für Gynäk., Bd. xxxii, S. 248, 1908).

The Pfannenstiel transverse incision, as shown by over 1000 cases, affords a better ultimate outcome than the longitudinal incision, even in cases with dubious asepsis. The tendency to post-operative hernia is less, the patients are able to be up earlier, and the scar is less prominent. Jaschke (Münch. med. Woch., Nov. 1, 1910).

Of 581 laparotomies performed during two years at the Tübingen clinic, Pfannenstiel's suprasymphyseal transverse fascial incision was employed in 550. Where great haste was indicated, as in a ruptured extra-uterine pregnancy, the median incision was used. Of the entire number, 84 could be re-examined. Of these, 3 showed herniæ in the scar. Of the entire number of cases, 418 healed without suppuration, 109 suppurated, and 23 died. R. Klotz (Zentralbl. für Gynäk., May 21, 1910).

EXPLORATORY OPERATIONS.—Very few exploratory operations should be done in abdominal surgery. The method no doubt makes diagnosis easier for the surgeon, but a more difficult matter for the patient, and it is highly important to make use of all available diagnostic resources before taking active steps in an operative way. Where an exploratory operation really needs to be done, however, it is best to make as small an incision as will suffice for the purpose. There are cases, for instance, in which we need to know if adhesions in the bile-tract region are complicating a loose kidney, or an appendix operation; and an exploratory operation, if small, for the purpose of determining that point is frequently in order. Then again, after traumatisms and perforations, the peritoneal cavity can contain blood, chyme, fecal matter or gas, which might be overlooked if one were too conservative about making exploratory incisions. In the presence of traumatic shock, ordinary diagnostic resources may fail us, and lead us to employ what older surgeons are apt to consider the resource of the tyro, namely, the exploratory incision.

PERITONEAL ADHESIONS.—Perhaps the most potent single factor in surgery of the abdomen relates to peritoneal adhesions. They lead to a large part of the constipation from which the public is suffering; to an extremely important part of the obscure dyspepsias; to various local areas of pain and tenderness, and frequently enough to acute disasters. The surgery of peritoneal adhesions belongs to the surgery of the future for the reason that such adhesions are commonly overlooked by diagnosticians at the present time, and only a trifling percentage of cases of gastric and bowel disturbances are placed where they belong in cause and effect relationship to adhesions. The new work of filling the stomach with bismuth solution and then making fluoroscopic examination to determine points of interference with gastric motility is now allowing us to make the diagnosis of gastric adhesions freely.

In post-mortem work we find peritoneal adhesions at some point in pretty much every abdominal cavity, in adults at least, and the argument that these have not caused trouble during the patient's lifetime includes

the idea that the patient is to have made the diagnosis himself, and to have informed his physician in the ordinary course of narration of his troubles. In this article the subject of peritoneal adhesions can receive nothing more than brief treatment, but it may be disposed of in a general way which includes most of the principles.

The surgeon has to consider the matter of separating peritoneal adhesions when they are found to give trouble, and to prevent their recurrence. He has to take steps in his operative work which will guard against the formation of adhesions resulting from his work. On the other hand, he has to resort to the use of peritoneal adhesions established for his own purposes in many parts of abdominal work. In cases in which we wish to make use of peritoneal adhesions it is important to scarify the peritoneum in the vicinity with the point of a needle in order to make sure of the free exudation of lymph together with destruction of part of the endothelial layer. The desirability of this scarification is experienced in laboratory work where one is working with animals, and it leads to the feeling that sometimes we do not obtain adhesions enough for safety in some kinds of bowel work, unless scarification has insured their production.

When we wish to prevent the re-formation of adhesions which had formed in advance of operation, many resources are of more or less value, but the author has chiefly depended upon two. These consist in the use of the aristol film, and the Cargile membrane made of the sterilized peritoneum of the ox. Aristol film is obtained by sprinkling aristol freely over the oozing surface from which adhesions have been separated, pressing the aristol upon these tissues firmly with a pad of gauze, and then leaving the area exposed to the air for a moment until the lymph-coagulum engages most of the aristol in its mesh. This presents a mechanical obstacle to the re-formation of adhesions. The author has found aristol in the tissues of animals after experimentation, several months after operation. This material probably disappears in time through slow liquefaction in the fat of cells which are undergoing retrograde metamorphosis.

To prevent the re-formation of peritoneal adhesions by using Cargile membrane, this material is laid upon oozing surfaces from which adhesions have been separated, and it may be caught at several points with strands of very fine catgut in case it does not adhere well enough naturally. Fingers and instruments must be very dry while applying this animal membrane; otherwise, it has a tendency to adhere to the fingers and instruments, rather than to the tissues of the patient. Cargile membrane is best transferred from a pad of dry gauze to the incised tissues. Animal membrane used in this way acts like the aristol film in presenting a mechanical obstacle to readhesion, but, unlike the aristol film, it has a tendency to undergo very rapid absorption in the peritoneal cavity, remaining sufficiently long, however, as a rule, to serve as a conductor for new endothelium beneath its protecting surface. Lubricating adhesion areas with sterile oil at the time of operation is favored by some surgeons, on the ground that per-

istalsis keeps oiled tissues moving too freely to allow of adhesions.

Adhesions for the most part undergo absorption by lymphatics under ordinary physiologic conditions, but where there has been much disturbance of tissue, infective or traumatic, the connective tissue which replaces the reparative lymph may remain permanently. It may act in various ways: by inhibiting peristalsis of the bowel and causing constipation, or exposing the patient to the danger of angulation of the bowel at adherent points. Adhesions may cause local irritation and discomfort only, or they may lead to complete strangulation of any of the tubular structures. They may become pulled out into long strands which ensnare the bowel, or which roll the omentum into abnormal positions, and they may prevent the normal gliding of viscera, and give rise to distant reflex disturbances.

In separating recently formed adhesions, it is best to separate them in as limited a way as will suffice for the completion of our work. The reason for this is because recently separated new adhesions are prone to re-form immediately in spite of all our efforts, and they may re-form in such a way as to be more injurious than when gradually arranged according to nature's plans.

To avoid the danger of formation of adhesions which were not present at the time of an operation we avoid rough handling of the peritoneum, which not only increases operative shock, but which stimulates the peritoneum to throw out an undue amount of lymph. The danger of the formation of such adhesions following traumatism produced by the operator is sometimes greater than the danger from adhesions which form under local septic conditions.

When in the course of operative work it becomes necessary to withdraw loops of bowel, omentum, or other intra-abdominal structures, it is important to prevent them from becoming dry, chilled or exposed to the vast numbers of bacteria constantly falling upon them from the air, and this is obviated by covering exposed surfaces with a thin sheet of rubber dam or of gutta-percha tissue while we are at work. Gauze as a protective agent is objectionable, because it injures the endothelial surfaces at once unless it is quite wet with saline solution, and has a special tendency to cause subsequent adhesion formation.

Some peritoneums do not form adhesions of consequence, even under marked provocation, while in other cases they appear despite all precautions. Consequently in abdominal surgery we must always have in mind the possibility of adhesion formation which may nullify our best efforts in an operative way. Traumatism of the peritoneum is particularly to be avoided when we wish to sponge out fluids from the peritoneal cavity, and this sponging can often be done between the fingers of the operator's two hands. He places his hands about the field which is to be sponged in such a way as to make a little well down to the fluid, and the assistant, carrying gauze into the abdominal cavity, brushes the gauze repeatedly against the fingers of the operator, rather than against the delicate peritoneum.

The two points at which we need to open the peritoneal cavity most

often for relief of adhesions are in the bile-tract region and in the cecal region. The incision for reaching adhesions in the bile-tract region is commonly made along the free border of the ribs over the adhesion area, and in the cecal region the ordinary incision for reaching the appendix suffices.

INTESTINAL SUTURES.—Operations on the intestinal tract, despite their number and variety, can be reduced to a few simple steps of technique of which the most important element is the application of sutures and other retentive apparatus.

In excision the principal stage of the operation is with the insertion of sutures. In primary anastomoses the application of the suture constitutes most of the operation. The cutting, consisting of making a communicating opening after the suturing, is partly done. A general outline of suturing and its substitute procedures is therefore necessitated.

To secure union in most wounds of the bowel a continuous suture of fine catgut is first passed through both mucous and muscular coats, and the peritoneum is closed over all with a continuous Lembert suture of fine silk.

Silk or linen thread are necessary for all sutures of the bowel which are to hold more than a few hours, for the reason that catgut is digested very quickly, if it enters the secreting glands of the bowel, and it is commonly taken up also with great rapidity by the peritoneum. This two-plane suture known as the Czerny-Lembert is the evolution of years of intestinal surgery, and is so firm as to prevent any possibility of leakage, but the apposition of the two peritoneal surfaces insures peritoneal union almost immediately.

In most cases it is best to scarify the peritoneum with the point of a needle wherever peritoneal adhesion is desired. This scarification with the needle insures the exudation of a large amount of reparative lymph. Any narrowing of the intestinal caliber under this suture is for the most part temporary, as expansion of the bowel will take place at that point later, and even the loss of a third of its circumference does not lead to actual stenosis.

Any operation which consists in the closure of a wound in the long axis of the bowel involves in general no different suturing. This applies also to certain operations for pyloroplasty and gastroplasty when a transverse incision is changed into a vertical one with a resulting increase of caliber. Whenever a cut surface of intestine does not enter into the restoration of continuity, it must be closed by a suture in the same way and under the same principle as linear wounds. Sutures of this type are applied to the cut surface of the stomach or intestine when these do not enter directly into anastomosis. In pylorectomy for cancer by Billroth's first method the cut stomach is simply sutured down to a point which makes the caliber the same as the caliber of the cut duodenum. A cut end of intestine may also be closed by Lembert sutures, for the principle remains always the same.

When two cut surfaces are to be directly united by so-called end-to-end anastomosis the double plane of suture is applied as before, but the exigencies here are such that it is sometimes advisable to insert some

of the peritoneal sutures first. Thus the serous sutures are placed for about one-half the extent of the opening to be closed; then the deep penetrating layer is inserted for the entire circumference, and finally the balance of the serous sutures are inserted.

This plan of suturing is followed in a great variety of procedures, and as a rule for end-to-end anastomoses and implantations and secondary suturing in general. In primary anastomoses the principle is the same, some of the suturing being done in the interest of accurate coaptation before the anastomotic opening is made. Thus, the parts to be joined having been placed in juxtaposition, with the fingers or with clamps, the two portions of gut are first joined by a number of serous sutures, about half the number to be required eventually. The opening is then made and the all-embracing layer of continuous catgut serves to unite the edges of the same, after which the serous suture is completed.

> To prevent small masses of mucosa from pouting beyond the suture line while invaginating the mucosa by the ordinary methods of suture, the writer passes the suture from the mucosa outward through all the coats of the intestine, instead of from without in, as is usually done. V. Schmieden (Zentralbl. f. Chir., April 15, 1911).

McGraw Ligature. — A loop of bowel is brought against the portion of stomach with which it is to be connected, and the two structures are fastened together with a continuous durable Lembert suture for a distance of two and one-half inches. The stomach and bowel are then fastened together with a McGraw strand of solid rubber introduced with a large needle, preferably the Hagedorn full-curve type. The needle is passed through the wall of the stomach to the lumen, and then brought out again at a point two inches away. The needle traverses the wall of the intestine in the same way. The rubber strand then being drawn tight is tied in such a way as to constrict the included parts as snugly as possible. The elastic-rubber knot is still further held by tying it with a strand of silk or linen. The next step completing the operation consists in approximating the portions of stomach and bowel which were left free after the preliminary suturing was done. The McGraw ligature was devised originally for gastroenterostomy, but is useful as well for enteroenterostomy.

Murphy's Button.—Wherever great speed in operating is a desideratum Murphy's button gives an advantage, and if it were not for the fact that buttons are sometimes retained, or that they sometimes give rise to complications *per se*, a very large part of our intestinal anastomosis work could be done with the aid of this ingenious resource.

Two-stage Operations.—Some of the procedures for establishing gastrostomy, enterostomy and colostomy are performed in two stages, the delay being for the purpose of allowing adhesions to form about the incisions and thereby protect the peritoneal cavity. Any operation whatever in which the external wound is not completely closed may become a two-stage procedure if a special operation is necessary to close the wound. As a rule, however, a considerable interval elapses in such cases, too long in fact to enable us to regard it as a single operative intervention. When wounds are closed outright there is a

possibility that they may at once require reopening for hemorrhage or sepsis. Hence, despite modern asepsis which has enabled us to operate so extensively in one stage, the abdominal operator is constantly exposed to the possibility of operating in successive stages.

SURGICAL DISEASES OF THE STOMACH.—We shall first enumerate the disorders in which surgical procedures are necessary, and then describe under a special heading the various operations resorted to.

Gastric and Duodenal Ulcers.—These require a variety of surgical procedures at various stages of their development. Recent or older ulcers may cause fatal hematemesis, perforative peritonitis, and crippling adhesions. From their location near the pylorus, actual or healed ulcers may cause pyloric stenosis. It must not be forgotten, however, that gastric and duodenal ulcer is a malady largely amenable to medical treatment, some forms not requiring surgery at all, but surgical intervention is indicated just as soon as medical resources lose efficiency, and at an earlier period than is customary as yet. The better diagnoses made by physicians in late years, and the extremely satisfactory surgery of the present day bring the question of time for operation to a point which can generally be agreed upon by expert physicians and surgeons.

Gastric ulcers are frequently multiple, and unless one is aware of this fact he may overlook others while caring for the first one which appears in the course of an operation. An active ulcer of the stomach may be surrounded by latent ulcers, or by scars which need excision, or which call for gastroenterostomy quite as much as the acute condition.

Perforating ulcer of the stomach is the one most often calling for immediate operation, while the chronic changes of the stomach due to scarring from old ulceration allow of more deliberate action.

The so-called bleeding ulcer without induration or tendency to perforation, while chiefly medical, sometimes calls for surgical relief, and it is sometimes very difficult to find the bleeding point; but, if the stomach is opened at a point not far from the pylorus, pressure of the finger upon various folds and rugæ or gentle wiping with a small gauze pad will excite hemorrhage anew. The arteries leading to this area may be ligated or separated, or, if the site is far enough away from the pylorus to avoid the danger of stenosis, a simple infolding of this part of the stomach wall with sutures results in putting this part of the stomach at rest out of the range of peristalsis, with a tendency to cure of the ulcer.

Even a chronic ulcer thrown out of the range of peristalsis by infolding of the stomach wall may sometimes go on to cure, but in the latter class of cases it is usually best to excise and to perform a gastroenterostomy. If the pancreas is involved in an operation for ulcer of the stomach, any escape of pancreatic secretion may cause local necrosis of tissues. Where the pyloric portion of the stomach is much scarred from old ulceration, or engaged in active ulceration, complete excision of this part of the stomach followed by some form of intestinal anastomosis is called for. Ulcer of the stomach at a distance from the pylorus causes some-

times hour-glass stomach through contraction of its scars, and the operation for this condition is referred to elsewhere.

Duodenal ulcer is the lesion met in nearly two-thirds of the cases personally seen. Unless an ulcer is demonstrated or hemorrhage requires it, operation is not advised. Gastrojejunostomy is done for duodenal ulcer; Finney's gastroduodenostomy for pyloric stricture. Proximal gastrojejunostomy or the whole area excised in hour-glass contraction. For calloused ulcer of the pyloric end partial gastrectomy is performed; the upper end of the duodenum is closed, and posterior gastrojejunostomy is performed independently. Of 234 patients operated more than two years before, 189 were cured, 21 improved, 10 were unimproved, while 14 died from various disorders. Mayo (Trans. Amer. Surg. Assoc., p. 142, 1908).

Of 205 cases in which operation for chronic gastric or duodenal ulcers had been performed the results two years after operation were as follows: Cured 148, relieved 5, doubtful 9, not improved 12; of 14 not heard from, 11 could be considered as cured. Deaths from operation 2, gastric cancer 7, various disorders 8. The following practical points: The operative treatment of stomach disorders should be confined exclusively to those cases in which an organic lesion is present. If one makes a diagnostic mistake, and displays upon the operating table a perfectly healthy stomach, gastroenterostomy should not be performed. In cases of acute perforation, the perforation should be closed or the ulcer excised. If the ulcer is prepyloric or duodenal, gastroenterostomy should be performed. If an ulcer is situated upon the lesser curvature, it should be excised to forestall the development of malignant disease. If an ulcer is prepyloric, pyloric, or duodenal, gastroenterostomy should be performed. When possible, the ulcer should be infolded, since hemorrhage and perforation have occurred from ulcers months or even years after the performance of gastroenterostomy. The most satisfactory method of gastroenterostomy is the posterior, no-loop operation, with an almost vertical application of the bowel to the stomach. Regurgitant vomiting occurs as a result of the loop operation, whether anterior or posterior. It is almost certainly relieved by enteroanastomosis. In slighter cases the vomiting of bile may be relieved by lavage continued for some weeks. Moynihan (Trans. Amer. Surg. Assoc., p. 129, 1908).

The various resources for giving gastric and pyloric ulcer a chance to heal spontaneously without excision of the involved area would often be preferable, were it not for the fact that cancerous degeneration of the embryonic blind tubules at old ulcer sites is a frequent occurrence.

An inexperienced operator had better attempt a primary anastomosis perhaps and risk the cancer. Jejunostomy purely for artificial feeding may be done to prolong life in cases where the patient is unable to withstand a prolonged operation. When the surgeon is first summoned after perforation has occurred, it is not only necessary to expose and suture the opening and cleanse the peritoneum, but it is often advisable to take advantage of the opportunity for performing a radical operation, if one is actually indicated. This is also the case oftentimes in emergency intervention for hemorrhage from an ulcer, and in penetrating wounds of the stomach it is further necessary to cleanse the peritoneal cavity in the vicinity.

Carcinoma.—The most radical procedures are indicated only when there is some expectation of cure. With early recognition and improved technique the operative mortality is

slowly diminishing, and operative procedures for comfort of the patient, rather than for cure within the three-year limit, are increasing in proportion. A preliminary laparotomy is often required to make a diagnosis of operability in cancer. It is often advisable to add a gastrotomy, as otherwise early malignant disease has been overlooked.

The only operation for radical cure is partial gastrectomy with extirpation of neighboring lymph-nodes. Since patients with well-recognized cancer of the stomach seldom live beyond a year and suffer greatly, palliative operations are indicated in theory, but it must be remembered that the mortality is rather high in such intervention. The resulting prolongation of life is also so slight that in ordinary cases the risk would hardly be worth while were it not for the considerable mitigation of suffering. When a palliative operation is undertaken, one with a minimum of intervention is indicated. Jejunostomy is therefore indicated on theory for artificial alimentation and complete rest of the stomach. In certain cases a gastroenterostomy may be preferable.

> The surgeon demands too much when he requests the practitioner to turn over cases of gastric cancer to him early, since diagnosis cannot be made sufficiently early. It were better if he were asked to turn over to him all cases of pyloric obstruction, without waiting for chemical analyses, which at best are uncertain, or for the effects of medicines, none of which relieve mechanical obstruction. Mayo (Jour. Amer. Med. Assoc., Aug. 15, 1908).

Congenital Stenosis of Pylorus.—Patients with this affection, even when severe, have been known to recover under medical treatment, while operation for radical cure has a high mortality, excepting at the hands of experts. Einhorn has recently devised an apparatus for dilating the constricted pylorus. If medical measures fail, gastroenterostomy is indicated early.

Hour-glass Stomach.—This condition is considered by some under the results of gastric ulcer, its usual causation. When it is discovered by exploratory laparotomy, or, better, with the fluoroscope, gastroplasty or gastrogastrostomy may be indicated, the former for enlarging the diameter of the constricted portion, and the latter for establishing a new communication between the stomach pouches when the first-named intervention is impracticable. Since some operators perform a secondary gastroenterostomy in such cases to avert the necessity for a possible second operation, it becomes a question whether a primary anastomosis is not the indication of choice. The latter in any case may be made with one or both stomach pouches, according to circumstances.

Non-obstructive or Atonic Dilatation.—Atonic dilatation of the stomach or gastric myasthenia, like pylorospasm and relaxation of the pylorus, is only a symptom of something else which needs to be worked out before we consider any operative work, but when the patient is losing ground in spite of other treatment, and we have pyloric obstruction due to kinking, a gastrojejunostomy or Finney's operation will make the work of the physician easier. Finney's operation is preferable in cases in which the gastric motility is not much impaired. Gastric adhesions involving the stomach lessen the

movements of the muscularis of the stomach, disturb circulation, and produce disturbances which predispose to ulceration, and a simple separation of these adhesions in some cases of chronic ulcer of the stomach or pylorospasm or relaxed pylorus obviates need of other treatment.

The operation of gastroplication, however, is usually performed for non-obstructive or atonic dilatation, with or without a secondary gastro-enterostomy; but there are very many cases of atonic dilatation which do not properly belong to surgery at all, and we must look for these conditions as reflex from some peripheral irritation, or some central nervous derangement. Atonic dilatation may result from exhaustion of the muscularis due to persistent attempts for years at overcoming partial obstruction at the pylorus, due to the presence of adhesions or ulcer scars. It may be due to the influence of distant peripheral irritation, such as loose kidney or eye-strain, or to fibroid degeneration of the appendix.

All these possible factors must be very carefully excluded one by one, and all three are at the present day generally overlooked by diagnosticians. Atonic dilatation occurring with certain psychoses, while belonging in the medical class, may nevertheless sometimes warrant surgical intervention.

Gastroptosis. — The operation of gastropexy or omentoplication for shortening the suspensory (gastro-hepatic) ligaments of the stomach is indicated in this condition, if the gastroptosis occurs singly, but it is apt to be associated with panptosis, due to relaxation of peritoneal supports of intra-abdominal organs; so that at the same time we usually need to shorten the suspensory ligament of the liver, repair a diastasis of the rectus muscles, and perhaps fix loose kidneys in place. This severe operation makes it advisable to accomplish all that is possible with external supports before resorting to operative procedures. Most of the patients with visceral ptoses are neurasthenics, and surgery is of temporary avail only,—to be avoided if possible.

Foreign Bodies.—Gastrotomy for the removal of foreign bodies is occasionally indicated, and does not differ from ordinary exploratory gastrotomy, excepting that the incision may be made very small in some cases, and just large enough to allow the entrance of forceps, which may be guided to the object through the aid of the fluoroscopic screen. This latter resource may also be used for reaching small objects in any part of the intestinal tract.

> Case in which 103 nails, 3 screws, 1 brass chain, 1 safety pin, and 1 sewing needle were removed from the stomach. The patient recovered, but five weeks later pains in the abdomen developed, particularly in the cecal region, which necessitated a reopening of the abdominal cavity. No more foreign bodies were found, but some adhesions were broken up. After that the patient remained free from pain, so that evidently the renewed pains were occasioned by the formation of adhesions in the abdominal cavity. Borchardt (Berl. klin. Woch., Feb. 21, 1910).

Stricture of the Esophagus.—Gastrostomy is required for some cases of stricture of the esophagus, to furnish access from two directions for dilatation purposes.

TYPICAL OPERATIONS UPON THE STOMACH.—Gastroplication. —This operation, which is intended

to reduce the size of the stomach by infolding its anterior wall, has been done successfully for simple non-obstructive dilatation, as well as for cases of pyloric obstruction due to the presence of bile-tract adhesions or ulcer scars. In several cases in which gastroplication seemed to be indicated because of dilatation secondary to the presence of adhesions, a simple separation of such adhesions, together with gastric lavage and massage subsequently, has allowed the stomach to regain its normal dimensions.

The principle of the operation involves the introduction of sutures placed within the seromuscular tissue. The more numerous and the longer the sutures, the greater the reduction in the capacity of the organ. The interrupted sutures are inserted at the lesser curvature, and passed in and out at intervals of one inch apart, until the anterior wall has been traversed without tying any sutures. They should be parallel in their course; the end sutures must not be placed so as to be in danger of constricting the lumina of the esophageal or pyloric orifices.

The sutures should be tied only when all have been placed in a row ready for knotting. If one suture were to be knotted in advance of, *i.e.*, before, the introduction of the next one, it would run the operator along in an undesirable plane, for mechanical reasons evident while one is operating. The anterior wall will be puckered, creased or reefed according to the technique used, with resulting restoration of the natural capacity of the stomach. The sutures may be inserted in series of superimposed planes when the dilatation is excessive.

After gastroplication a cross-section of the organ shows a series of plaits if one plane of sutures is used; while, if several planes are superposed, a sort of diaphragm projects across the cavity. These formations tend to undergo some atrophy. Although the normal size of the organ is restored, the shape is not, and the tendency of the posterior wall to pouch must sometimes be offset by a posterior gastroenterostomy. It has even been counselled to perform the latter as a matter of routine.

A form of gastroplication has also been performed for gastric ulcer. The reef of the stomach wall which is the seat of the lesion is thus placed in relative rest, and under appropriate medical measures the ulcer may disappear during the atrophy. Two suture points usually suffice. Naturally the operation is best suited to ulcer of the anterior wall.

Gastric Omentoplication.—Gastric omentoplication may be mentioned in this connection. This operation consists in taking a tuck in the suspensory ligaments of the stomach, and is indicated in gastroptosis. These portions of the lesser omentum known respectively as the gastrohepatic and gastrosplenic ligaments are sutured in three superposed planes with mattress sutures, the deepest being inserted for a very short distance, one-half inch to one inch near the pylorus. The next plane projects well beyond the confines of the first, while the third corresponds to the amplitude of the tuck to be made. The sutures are then tied in the order of insertion. It must be borne in mind that the aim of omentoplication is to secure elevation without

compromising the mobility of the stomach.

Gastrotomy.—Incision of the stomach is indicated primarily for exploration of the stomach, and at the same time when required for the removal of foreign bodies, tumors, etc., checking hemorrhage, and dilating strictures at either orifice. It is always desirable after the laparotomy incision to examine the stomach thoroughly from without before incising its wall. The technique for incising the stomach is practically the same in different operations, although the site and extent may vary with the condition to be treated. The usual incision is made in the long diameter as far as possible from large blood-vessels, and is not less than three or more than five inches long. It is advisable to wash out the stomach before operation, but when this for any reason has not been done the organ must be evacuated by sponging gently with gauze or flushing with a siphon. Before incision the stomach must have been walled off from the peritoneal cavity with gauze. After the purpose of the operation has been fulfilled, the gastric incision is closed with one or more planes of continuous silk or linen sutures of the Lembert type.

When gastric ulcer is present some additions to the technique may be required. When the operation has been undertaken for hemorrhage from the ulcer, the latter must, if possible, be excised, and if an ulcer is found it is always best excised irrespective of the question of hemorrhage. It may, however, be impracticable to excise, from the position of the ulcer, or because of multiple ulcers or bleeding points, or the source of the hemorrhage may be obscure. Under such circumstances hemostatic procedures may be unavailable, and may even aggravate the state of affairs. The only resource in such cases is to perform gastrojejunostomy. Whenever an ulcer can be excised, the wound is closed first with catgut sutures, and a Lembert silk or linen serous suture must be superposed.

When the ulcer is seated on the posterior wall with implication of the serous coat, it can hardly be dealt with through the anterior incision, and therefore an incision must be made through the transverse mesocolon, and the posterior wall of the stomach brought into view. When the pylorus is the seat of the ulcer, simple excision will be inadvisable because of subsequent stenosis, and pyloroplasty will be indicated. When there is, besides, any evidence of esophageal stricture, great care should be taken to perform gastrostomy by a typical method, unless there is a possibility that the obstruction can be relieved and the treatment completed from above. It would be impracticable to turn an ordinary gastrotomy incision into a gastrostomy fistula.

Pyloroplasty (Heinecke-Mikulicz Operation).—This operation consists in restoring the original caliber of the pylorus when it is the seat of a simple stricture, or when suture following excision of an ulcer would result in pyloric stenosis. As cicatricial stricture of this orifice is due usually to the healing of ulcers, the operation is practically associated with this condition. Only a single procedure known as the Heinecke-Mikulicz operation is current in the narrower sense of the word, as other operations to which

the name is given are in part gastroduodenostomies.

The technique is as follows: The stomach having been exposed by a median incision, the pylorus is drawn out, walled off from the peritoneal cavity, and incised. The presence of adhesions renders this stage difficult and sometimes furnishes a contraindication. The incision may be made after an assistant has approximated the stomach and duodenum, each at a point some three inches beyond the stricture. The incision while made in the long axis of the pyloric end, extending from duodenum to stomach, is really made from following the pyloric curve, of a horseshoe shape. Any redundant tissue is excised. If a fresh ulcer is present most authors prefer to do a gastroduodenostomy. In order now to enlarge the pyloric lumen, forceps applied to the middle of each lip of the wound are made to pull it into a straight transverse incision. In this position it is sutured in two planes including the peritoneal layer, unusual care being required because the incision is not sutured in its original plane.

Despite the recommendations of Mikulicz and other eminent surgeons, the operation has many drawbacks. Adhesions are likely to result, and whether from this or other causes the stenosis may reappear. The indications therefore are, as a rule, better carried out by performing some form of gastroduodenostomy or pylorectomy.

Pyloroplasty by Finney's (Gould's) Method and Gastroduodenostomy.—In both of these procedures an anastomosis is made between the stomach and duodenum, but the objects are entirely unlike, being in Finney's operation the widening of a stenosed pyloric orifice, while in the latter the pylorus is excluded outright by a short circuit. Gastroduodenostomy does not differ essentially from gastroenterostomy in general save that the duodenum must be mobilized beforehand. As that step is also required in Finney's pyloroplasty, the latter alone needs a detailed description.

The operative success will be due to the mobility of the duodenum, which may be and usually is more or less immobilized by secondary adhesions, and to such extent sometimes as to appear inoperable. Aside from adhesions the anatomic relations may be such as to require considerable operative manipulation to make the parts accessible, sometimes division of gastric ligaments. Traction sutures may then be inserted outside of the area to be incised for the purpose of steadying and tightening the tissue, but here it is better to use clamps, as in Gould's modified operation, which brings pyloroplasty in the same class as other anastomoses. The clamps grasp the duodenum and stomach in the long diameter—not in the transverse diameter, which would be the case in an exclusion of short-circuit anastomosis—with one clamp securing the duodenum and the other the stomach just above the greater curvature; the two are brought side by side and the two portions of intestine united by continuous seromuscular sutures. A U-shaped incision is now made, the bend of which corresponds to the pylorus. Redundant mucous membrane is clipped off; the resulting diaphragm or tongue is overcast with a second row of continuous sutures, simple

communication now being established between the duodenum and stomach at the natural orifice. An elliptic space remains to be closed with two planes of sutures, one all-embracing and the other serous and muscular.

Gastrostomy.—*Hacker's Operation.*—This procedure is rather a small gastrotomy left unsutured than a true gastrostomy, in the modern sense of the term. It is recommended chiefly in emergencies. The stomach having been exposed and temporary traction sutures passed through its wall to steady the organ, two planes of permanent sutures are inserted on either edge of the wound. The first plane passes through the abdominal wall only, including the peritoneum; the second, placed just within the others, includes in its grasp the walls of the stomach, but without entering the cavity. The sutures are then tied and cut close, so that the stomach is fixed to the abdominal wall. Additional smaller sutures are left in place, and the wound packed with gauze.

At a subsequent period, usually the following day or the second day, the wall of the stomach is opened with a knife, the wound being one-half inch long or just the size to contain a tube which should fit closely. The traction sutures should now be withdrawn. The abdominal incision for this operation should be three inches long and vertical in direction, slightly over an inch to the left of the linea alba, and beginning about one inch beneath the costal arch. When the rectus muscle is exposed the anterior fascia is divided with the scissors, but the belly of the muscle is separated bluntly. The posterior layer of the sheath is again divided with the scissors, exposing the peritoneum. This is opened only sufficiently to admit the finger, but subsequently prolonged with blunt scissors, and the peritoneum and muscle sutured with catgut.

Franck's operation is a so-called valve operation, in which the portion of stomach wall to be incised is passed out of a relatively large orifice under a bridge of skin, and finally out of a smaller incision, in which locality it is incised.

The layer incision is known as Fenger's and runs parallel to the costal arch and about one inch below the latter, starting to the left of the ensiform cartilage and not exceeding two inches in length. When the parietal peritoneum is divided it is sutured to the muscles of the abdominal wall. With two fingers in this opening the anterior wall of the stomach is drawn out and the apex of the resulting cone transfixed with a traction suture, while a running silk suture unites the base of the cone to the edges of the wound, all the tissues being embraced except the skin and the gastric mucosa.

The lesser incision is parallel to the first and seated an inch above the margin of the costal arch. Its length should not exceed one inch. The tissues between the two incisions are then detached from the subcutaneous structures, when with the aid of the traction suture the apex of the cone is drawn under the bridge of skin and out of the lesser opening, to the edges of which it is sutured. The major orifice is then closed and the apex of the stomach cone opened, a tube being placed within the canal. The Fenger incision may be replaced by a vertical one, as advised by Robson and others.

Witzel's Operation. — The canal, which acts as a valve, passes obliquely through the wall of the stomach. The anterior surface of the latter is exposed in the usual manner and sutured to the wound; an opening is then made in the central portion, toward the greater curvature. Into this a soft catheter is passed; the portion outside the stomach is laid flat against the latter, and directed downward and outward.

Sutures are now passed through the seromuscular coats of the stomach over the tube and through the opposite side so that when tightened the tube is covered by a fold of stomach wall. The first suture point is seated one inch from the opening in the stomach and the entire length of the canal should be about an inch and a half. The abdominal wound is closed down on the free end of the tube, which is left projecting.

Kader's Operation.—The tube enters the stomach directly instead of obliquely, and the canal is formed by producing an artificial thickening of the stomach with certain planes of suturing. Thus with the tube *in situ,* two folds of stomach wall are formed by inserting sutures twice through the wall—one to each side of the tube. These are tightened and cut close, and similar sutures are next inserted just outside the first. Each plane comprises four sutures. The canal thus produced is about half an inch long and has a good valvular action.

A similar canal may be produced by several planes of purse-string sutures, as recommended by the late Dr. Senn.

Author's Operation.—The author constructs a fistula lined with epithelium, by utilizing long skin flaps. At the left costal border, over the chosen stomach region, make an incision five inches long through the skin and subcutaneous tissues directly cephalad from the costal border. Make a similar incision on either side of the first incision, giving two ribbons of skin each one inch in width. A transverse incision at the cephalad end of the parallel incisions frees the ends of the skin ribbons. The skin ribbons are next freed throughout their length, but remain attached at the costal border. The epithelial surfaces of the skin ribbons are placed in apposition and a running suture of catgut unites their margins. This transforms the ribbons into a tube of skin. The stomach is exposed and opened. The free end of skin tube is sutured with silk to the mucosa of the stomach. A rubber tube is passed through the skin tube. One end of the rubber tube is to remain in the lumen of the stomach until repair of the wound is complete. The other end of the rubber tube emerges from the skin tube on the abdominal wall, and serves for introducing nourishment. When the skin tube with its contained rubber tube follows the stomach into place, the remaining structures to be sutured have fallen together in such a way that the character of final suturing is apparent, and needs no description. After repair of the wound is sufficient, at the end of a few days, the rubber tube is removed. This leaves a fistula lined with epithelium extending between abdominal skin and stomach mucosa. The stomach has drawn the skin tube into position at such an angle that atmospheric pressure keeps the skin tube closed, excepting at times when food is to be introduced.

The writer makes an incision in the abdominal wall in the median line, from the tip of the xiphoid cartilage downward 3 or 4 inches. The left hand is then introduced into the wound and the abdominal wall on the left side grasped between the middle finger and thumb. In this way the left rectus muscle is located. With a long tenotome an opening is made through the substance of the left rectus from the wound surface to emerge on the skin surface a few centimeters within the outer border of the rectus. This opening is widened by cutting upward and downward and dividing the rectus into two equal layers, an anterior and a posterior. The size of this passageway should correspond to that of the portion of the stomach which is to be drawn through. This portion of the stomach is then drawn through with a suitable forceps and its base sewed to the posterior edge of the median end of the passageway with 3 catgut sutures. The opposite surface of the base is then sutured to the peritoneum and rectus on the opposite side of the median wound. The deep edges of the upper and lower portions of the median wound are then brought together by sutures. The end of the projecting portion of the stomach is now conducted through the tunnel made for it in the rectus muscle and skin, and its apex is fastened to the skin edges of the small lateral external opening. The large median wound is then closed over the projecting portion of stomach by two layers of sutures, one for the fascia and the other for the skin. Finally, the emerging end of the stomach is opened and its edges sutured to the skin. This portion provides a strong, permanent sphincter for the gastrostomy opening and makes it continent. Lafaro (Deut. Zeit. f. Chir., Bd. cviii, S. 307, 1911; Amer. Jour. Med. Sci., April, 1911).

Gastrorrhaphy.—The operation comprises working beyond an emergency suture of the stomach wall for traumatisms, the latter including perforation from gastric ulcer. But since gastrorrhaphy is involved in suturing a gastrotomy wound there is little to be said under a special heading beyond the statement that some modifications arise from the nature of the injury. While the operation is readily performed after incised and lacerated wounds, but few victims of such injuries recover —practically none after gunshot wounds. The technique of closing stomach wounds is described with gastrotomy.

Report of 218 cases from the operative clinic at Rochester from January 1, 1905, to April 1, 1909. Eight were from the duodenum, and of these all were simple ulcers. The remaining 210 were from the stomach. Of these, 47 were ulcers without suspicion of carcinoma, 2 were sarcomas, 2 adenomas, and 1 a diverticulum. Of the remaining 158 in the stomach, 5 were ulcers with enough microscopic appearance to place them in the doubtful class as possible transition cases. Of the remaining 153 cases, which were undoubted carcinoma, 109, or 71 per cent., presented sufficient microscopic evidences of previous ulcer to warrant grouping them as carcinoma developing on previous ulcer. Whereas, theoretically at least, it has been considered probable for many years that there was an immediate relationship between gastric ulcer and carcinoma, the profession has never before been treated to a paper so convincing, both because of its source and because of its individual excellence. Generally speaking, the writers show that a little more than two-thirds of a very long series of carcinomas undoubtedly took their origin in pre-existing ulcers. Wilson and MacCarty (Amer. Jour. Med. Sci., Dec., 1909).

Report of 12 successive perforations of the stomach or duodenum with 11 recoveries, in which great importance was attached to rapid operation; no irrigation; multiple drainage (one tube to the site of perforation, a second and third in the right and left lumbar

region, and a fourth in the suprapubic region if fluid exists in the pelvis); elevation of the patient's body; early feeding by the mouth and continuous **saline irrigation by rectum** immediately after operation. Carwardine (Lancet, vol. i, p. 239, 1910).

According to the author's experience, the prognosis in perforating gastric and duodenal ulcers is fairly good if operation be resorted to during the first twelve hours when the pulse rate does not exceed 100, while it is quite unfavorable if the pulse is 120 or over. As regards treatment, suture of the perforation after excision of the margins of the ulcer or of the entire ulcerated area and very gentle removal of the exudate from the abdominal cavity are indicated in suitable cases. This should be followed by gastroenterostomy only in patients operated on during the first twelve hours in whom the general condition is comparatively good and when the history reveals undoubted symptoms of pyloric stenosis or where the pylorus is found to be stenosed. Of the ulcers observed 94 were localized, 76 to the stomach and 18 to the duodenum. No better illustration of the importance of early operation is afforded than the fact that two-thirds of the cases operated upon during the first twelve hours recovered. G. Petren (Beiträg. z. klin. Chir., Bd. lxxii, Hft. 2, 1911).

In the treatment of severe gastric hemorrhage Rovsing's method, which the writer has employed since two years, has proved very serviceable. It consists of the introduction of a diaphanoscope, an especially devised instrument, through an incision in the stomach, thus permitting of direct inspection of its walls. This method permits of the detection of very small ulcerations, no larger than a pea, while any bleeding vessel can usually be seen. The hemorrhage is arrested by applying a ligature, taking in the entire thickness of the stomach wall, and this area buried by one or two purse-string sutures. After removal of the diaphanoscope the gastric wound is sutured. In 4 or 5 cases of severe hemorrhage this procedure caused arrest of the bleeding. L. Kraft (Archiv f. klin. Chir., Bd. xciii, Hft. 3, 1911).

Gastroplasty.—Gastroplasty is a procedure which is indicated only in hour-glass stomach, and differs but slightly from pyloroplasty, the constriction of the organ taking the place of the pylorus. As in Finney's pyloroplasty, the two portions of the stomach are first brought together by sutures or clamps and a horseshoe incision made around the suture line at a distance of one-fourth inch. The inner or posterior edge of the wound having been stitched by a continuous suture, the outer or anterior edge is similarly treated. The communication between the two halves of the stomach is thereby greatly amplified. Reinforcing sutures will probably be required for the anterior sutures.

Gastroplasty may also be performed along the lines laid down for the Heinecke-Mikulicz pyloroplasty, in which a transverse incision is changed to a vertical one.

The value of the operation is in question.

Gastrogastrostomy.—Like gastroplasty the operation is indicated only in hour-glass stomach. It consists of a simple anastomosis between the halves of the stomach, which then possesses two distinct communicating passages. The two stomach pouches are sutured together with a continuous Lembert silk suture along one side. The two pouches are next incised, and the cut surfaces joined as in gastroenterostomy, and final suturing completes the apposition of the pouches.

Partial Gastrectomy.—Partial gastrectomy, the name of which is self-

explanatory, is undertaken chiefly for cancer of the pylorus, and to a certain extent for cancer of the stomach proper, gastric ulcer, and hour-glass stomach. When performed for benign ulceration the cases selected are those near the pylorus when the lesion is unusually large, indurated or multiple. When done for hour-glass stomach the constriction between the stomach pouches is the seat of an ulcer, and the excision can be combined with gastrogastrostomy.

Technically the mere excision of a bleeding ulcer anywhere in the stomach is a partial gastrectomy, but in the typical operation the pylorus must be sacrificed, and therefore the continuity of the digestive tube must be restored by some form of gastroenterostomy, either gastroduodenostomy by end-to-end anastomosis, a gastroduodenostomy by implanting the duodenum in the stomach wall, or an ordinary gastroenterostomy. Partial gastrectomy has been divided into a typical and a cylindrical method, but the former, which relates only to incision of ulcer areas in the stomach proper, is sufficiently comprehended under gastrotomy. Cylindrical gastrotomy is also termed pylorectomy, since the pylorus is always excised completely, alone or with more or less of the entire continuous gastric wall. Over a third of the organ may thus be sacrificed.

Billroth's Operation.—The original method practised by this surgeon was to excise the pylorus and the necessary portion of the stomach wall, and to suture the cut end of the stomach until it reached the size of the duodenum. The two cut ends were then joined by end-to-end anastomosis. At a later period the same surgeon preferred to close up both cut ends and perform a posterior gastrojejunostomy.

Billroth prefaced his pylorotomy by ligating the vessels of the greater and lesser curvatures, and next tied off the peritoneal attachments (gastrohepatic and gastrocolic ligaments). This mobilization enables the pylorus to be drawn out of the external incision. Clamps are then applied to either side of the pylorus, two pairs each to duodenum and stomach, at a distance of an inch from the diseased area. Fingers or clamps may be used on the proximal sides. The stomach and then the duodenum are divided between the clamps. The divided end of the stomach is sutured, after complete hemostasis is secured with a running suture of chromicized gut, passed through-and-through on each side in order to secure some inversion. The suture is carried from above downward to such a distance that the unstitched portion corresponds in size to the cut surface of the duodenum. A second through-and-through suture plane is added and serves to further invert the wound edges.

The duodenum is not divided until the stomach has been sutured. The two divided ends are now partly joined by a continuous Lembert suture, leaving room to apply an infolding through-and-through suture of chromicized catgut within the plane of the outside suture, which latter is then completed.

Kocher's Operation.—In this method the cut end of the stomach is completely closed while the cut end of the duodenum is implanted into the posterior wall of the stomach. The pylorectomy itself does not differ

essentially from that of Billroth. The divided end of the stomach is completely closed by two planes of sutures, an inner continuous through-and-through suture of chromicized gut, and a Lembert suture outside of it. The essential part of the operation consists in the gastroduodenostomy by which the cut edge of the duodenum is implanted about two inches behind the closed wound of the stomach. The duodenum held in position with fingers is first made fast to the stomach by a running Lembert suture inserted at the point of contact with the stomach and occupying one-half of the gut just back of the cut edge. The stomach is then incised just beyond this suture line in such manner that the two edges may be exactly approximated. The anastomosis is now made with a continuous interior suture of chromicized gut, and the original outside suture is completed. The interior anastomosis suture is inserted by the through-and-through method, and traverses all the coats of the intestine.

Hartmann's operation differs from the preceding in that it includes extirpation of the lymph-nodes which are seated within the gastrohepatic ligament. It is therefore only applicable to cancer of the pylorus in a more or less advanced but still operable stage. The operation proper and its termination by gastroduodenostomy or gastroenterostomy is not different materially from the preceding.

Mayo's operation is also a radical procedure, and involves not only extirpation of lymphatics draining the pyloric area, but an unusual degree of removal of stomach, including all the lesser curvature. The stomach is closed entirely, and continuity restored by any of the methods in vogue.

The mortality if lowered (1) by protecting the operative field against the escape of gastric contents during the operation; (2) by using a combination of morphine, hyoscine, and chloroform for narcosis, thus reducing the likelihood of pneumonia; (3) by limiting the operation to patients in whom the hemoglobin percentage is relatively high. In such cases the stomach may be resected some centimeters beyond the disease. Czerny (Annales Intern. de Chir. Gastro-Intes., vol. ii, p. 61, 1908).

Review of 266 partial gastrectomies involving the pyloric end of the stomach performed in the Saint Mary's Hospital, Rochester, between April 21, 1897, and Jan. 27, 1910. There were 34 deaths from the operation, a mortality of 12.4 per cent. Some of the patients are still living eight years after the operation. The writer does not believe the pessimism as regards this operation to be justified by the facts. He calls attention to two important indications for operation in gastric cancer: 1. Food remnants found repeatedly in the stomach after twelve hours should, when taken in connection with the clinical history, call for a surgical consultation, which in a large majority of cases will lead to an exploratory operation. 2. The finding of a movable tumor in the pyloric end of the stomach cannot be overestimated as to its surgical significance. Gastric cancer by itself does not give, he is convinced, characteristic symptoms during the curable stage. But if it is situated in the pyloric end of the stomach mechanical conditions are early induced which afford most valuable information. An effort should always be made to remove the lymphatic area, whether diseased or not. It must be removed before the lymphatics are infected. Prophylaxis of gastric cancer can be aided by the excision of calloused gastric ulcers, which are its origin in 70 per cent. A typical resection necessitates the re-

moval of all that part of the stomach lying to the right of a line dropped vertically from the cardiac orifice, though in some cases more of the fundus must be removed on account of the direct extension of the disease. As a general rule, it will be most convenient to make the separation of the superior border of the stomach first, beginning the operation by (*a*) ligation of the superior pyloric vessel, (*b*) the gastric, (*c*) the felt gastroepiploic, (*d*) the gastroduodenal vessels. As each vessel is secured, the glandular separation is effected. In doing the anterior gastrojejunostomy he usually follows the method of Hartmann, *i.e.*, the two-row suture method with slight modifications. Generally speaking, the Kocher method of joining the jejunum to the stomach is not so satisfactory as the Billroth No. 2 method, *i.e.*, closing both the end of the duodenum and the stomach and making an independent gastrojejunostomy. When the patient is in good condition the operation has an operative mortality of under 5 per cent. In advanced cases, the resection is worth the risk, considering the short lease of life of patients left without it. W. J. Mayo (Jour. Amer. Med. Assoc., May 14, 1910).

Complete Gastrectomy.—This operation, including subtotal gastrectomy, is now practicable as a method, and has radically cured perhaps a very few individuals of cancer, but is seldom attempted, the operative mortality being very great and cases suitable for such intervention seldom recognized in time. Removal of the stomach is not a difficult operation at all, but search for and removal of lymph-nodes must be very thorough. The removal is followed by an end-to-end anastomosis made between the duodenum and esophagus, or the cut end of the former may be closed and the esophagus implanted into the jejunum. The author has found it much easier to do the work if a small part of the cardiac end of the stomach is allowed to remain.

In 76 cases of cancer of the stomach during the last ten years, the growth was inoperable in 21; in 11 cases a radical operation was undertaken. Of these, 7 were completely cured; in the other 4 the operation was attempted as a last resort without much hope of permanent success. In the cured patients nine-tenths of the stomach had been removed; the age of the patients ranged from 38 to 75. Direct anastomosis between the stomach and duodenum was possible in all but 1 of these cases; 2 of this group of 7 cured patients have succumbed since to an intercurrent affection. The others are in good health to date, the postoperative life being over five years in one instance. Boeckel (Bull. de l'Acad. de méd., Oct. 4, 1910).

Case of complete gastrectomy in a man aged 43. The whole organ was removed. The cut end of the esophagus was stitched to the side of a loop of jejunum. The patient made a good recovery from the operation. During the three years and eight months that he lived after the operation he was under constant observation. He was perfectly well up to the early part of the year 1910, when he began to show the evidences of a profound anemia. He was strikingly pale and breathless, and he lost weight. Under treatment, however, he improved, and in May, 1910, his color had returned and he was able to ride and drive and attend to matters on the farm. In August, 1910, he began to fail again; he became easily tired, though he still tried to carry out the greater part of his work. His appetite remained good and he had no indigestion. In October, the signs of anemia reappeared, he grew much weaker, and had to cease work. He began again to lose weight, his appetite vanished, and he vomited occasionally. There were no abnormal signs of any kind in the chest or abdomen throughout the illness. Soon after Christmas, 1910, he had to take to his bed, and he died on the last day of January,

1911. He had gained 38 pounds after the operation, and he held the gain for nearly three years. His appetite was good, he experienced the sensation of hunger, and he was able to eat ordinary foods. Moynihan (Lancet, Aug. 12, 1911).

SURGICAL DISEASES OF THE PERITONEUM.—Septic Peritonitis.—This condition being in the great majority of cases secondary to some suppurative process either within or without the peritoneal cavity, the treatment cannot be considered independently of that of the primary condition, which consists fundamentally of incision and drainage of or removal of the pyogenic focus. The conditions likely to give rise to peritonitis are separately mentioned. If the focus is outside the peritoneal cavity, the latter need not necessarily be opened, because the peritoneum rapidly guards itself by hyperleucocytosis after a focus of infection is cared for. If the focus is in the peritoneal cavity, it may or may not be advisable to treat the peritoneum actively. If the peritonitis comes from an intestinal perforation an enterorrhaphy may be required, but it is often safer to make temporary drainage, and fistulæ following have a tendency to close spontaneously. Other cases may require excision, as when a portion of the gut is gangrenous. In many cases, however, posture and drainage alone are indicated, and any unnecessary handling of the peritoneum is to be deprecated. Only when drainage cannot offer a prospect of self-limitation of the process is a thorough cleansing of the peritoneum indicated, and this is best accomplished by flushing with **hot saline solution** through short incision, and the glass tube.

Results obtained in 100 well-marked cases of diffuse septic peritonitis resulting from inflammation of the vermiform appendix. The cases were treated by the author and by George R. Fowler. Sixty-seven of the cases recovered. Of the 33 deaths, 17 occurred within twenty-four hours of operation. The salient points in the treatment of these cases were: A small incision and the avoidance of eventration; thorough cleansing of the primary focus of infection and removal of the appendix. Evacuation and cleansing of all accessory abscess cavities and the pelvis before washing out the peritoneal cavity. A rapid systematic flushing of the peritoneal cavity with **sodium peroxide solution** followed by **hot saline.** The continuance of the saline flushing until the sutures are placed, and for the most part tied. The provision of proper drainage of septic fluid into the pelvis, of a large glass tube containing a capillary drainage strip emerging through the lower angle of the wound or, in females, by a large-caliber rubber tube filled with wicking passed through a posterior colpotomy incision. The drainage of accessory abscess cavities with gauze or wicking. The elevation of the head of the bed to accelerate the drainage of septic fluid into the pelvis, where it can be removed through the glass tube, or, in case of vaginal drainage, find a ready exit. R. S. Fowler (Med. News, May 28, 1904).

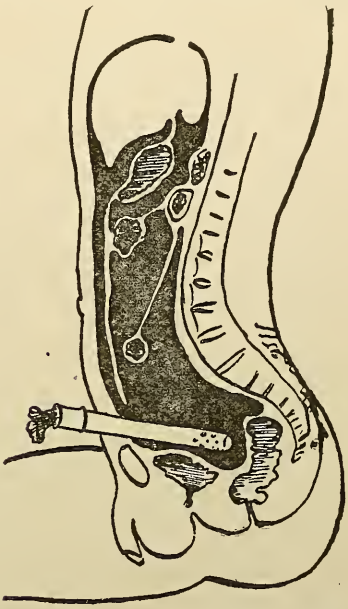
Murphy's treatment consists in making a small opening in the abdomen, doing such operation at the point of origin of the peritonitis as is required, the introduction of a large drainage-tube into the pelvis, placing the patient in a sitting posture of 35 to 40 degrees, and the administration of a **salt solution** every two hours per rectum. An important feature of the treatment is to avoid handling the intestines or peritoneum more than is absolutely necessary. It is remarkable how much salt solution is absorbed and how it increases elimination by the kidneys. As much as 18 pints of water may be administered by the rectum in twenty-four hours and all

retained; this is only accomplished, however, by elevating the douche bag but eighteen inches above the bed and allowing the solution to flow into the bowel very slowly. The rectal tube can be kept in twenty-four to forty-eight hours. Water should also be administered by the mouth. Gibbon (New York Med. Jour., April 7, 1906).

The mortality of general peritonitis of but a few years ago (65 per cent. in 1069 collected cases between 1888 to 1904, 55 per cent. in 400 cases between 1900 to 1904, 50 per cent. in the Mayo clinic) is remarkable in its contrast with that of J. B. Murphy in December, 1906, *i.e.,* 38 consecutive cases with but a single death, and that from pneumonia on the sixth day.

It was Murphy's protest against general irrigation of the abdomen, showing that the higher mortality rested with those who used it, that first attracted the attention of surgeons. His first paper dealt with 5 cases (including 1 typhoid case) without a death, was followed in October, 1906, with 28 cases with 1 death, and up to his last paper includes 48 consecutive cases with only 2 deaths. These astounding results have been recently also confirmed in England. Moynihan states that, in his opinion, and as a result of a fairly large experience of the method, "there are few therapeutic measures equal to it," and Cawardine considers it "the most valuable suggestion of recent times."

The principles laid down by Murphy are: 1. Operate early. 2. Operate quickly. Murphy gives ten minutes as the average time in which to close the gastric or duodenal opening, or to remove the offending appendix or tubes. 3. The anesthetic must always be ether, if the patient can stand it; if not, then a local anesthetic. Stiles's work has shown how dangerous chloroform is in acute suppurative conditions, in the production and retention of acetone. 4. It is a fatal mistake to mop, wash, or handle the intestine. The peritoneum is essentially an absorbing surface; carmine granules injected into its cavity are rapidly absorbed, especially in its upper half, and conveyed by the lymph-stream to the general circulation. Organisms similarly do harm by the rapid absorption of their toxins in a similar manner. Lymph, like any other granulating surface, is protective, and tends to prevent this absorption. All undue manipulation of such lymph-covered surfaces, or lymph removal by sponging, washing, or mopping, will increase, therefore, the danger of septic absorption. 5. The Fowler position



Peritonitis treated by the Murphy method.

and a suprapubic drain. The object of the Fowler position is to allow the discharges to gravitate toward the pelvis, and away from the danger zone of the diaphragm. The patient, as soon as he has recovered from the anesthetic, is placed in the sitting posture, so that the abdominal cavity is vertical in position, and drainage is instituted by placing a large drain in the pelvis through a stab wound above the pubis. This drainage-tube is three-fourths to one inch in diameter, about eight inches long, glass, and goes down to the pouch of Douglas in the female, and the rectovesical in the male. In this position the tube is almost horizontal; and if it is filled

with fluid, each excursion of the diaphragm will pump a small quantity of it out into the dressings. The hole is now at the most dependent part of the abdominal cavity. 6. **Proctoclysis** or the absorption of large quantities of saline by the rectum for the first two days after operation. As soon as possible after the operation, a tube having numerous holes in it and one-half inch in diameter is inserted into the rectum for about two to three inches. This is connected by means of a rubber tube of the same diameter with a container suspended from four to twelve inches above the plane of the patient's couch, and the whole is filled with warm saline. By means of this head of water (it need only be four to six inches in height, as a rule) saline gradually trickles into the rectum at about the rate of three-quarters to one pint an hour. The temperature of the saline is kept at 100° F. and should never reach 106° F., or it will not be retained. The object is not for the saline to act as an enema, but to be given so slowly that it is absorbed as fast as it flows in. If the patient feels a desire to defecate, it means that the rectum is becoming so distended that the head of water is too great, and that it must be decreased. Should the desire become overwhelming, then the saline is shut off for a time until the desire disappears. R. E. Kelly (Liverpool Medico-Chir. Jour., July, 1909).

Out of a series of 167 cases of diffuse septic peritonitis from appendicitis operated on by the writer at varying intervals following perforation up to January, 1909, there were but 15 patients operated on within twenty-four hours of the onset. Patients with diffuse septic peritonitis from appendicitis operated on within twenty-four hours of the onset of the disease, *i.e.*, before the peritoneum is infiltrated, recover, providing the primary focus is removed quickly without damaging the absorbing power of the peritoneum, irrespective of feeding or enemas, providing the absorbing power of the peritoneum is properly used. Fowler (Surg., Gynec., and Obstet., Nov., 1909).

The writer treated some 15 cases of diffuse peritonitis with intravenous injections of **adrenalin**. In every instance, there was a marked improvement in the pulse for a short time; but this disappeared in a few minutes, and in one or two hours the effect had passed away. In a few patients, the increased pressure in the vessels continued, and these patients recovered. The symptoms, however, were indistinguishable from those which follow an injection of normal saline solution. These results coincide exactly with the experiments upon animals. Adrenalin is well known to excite an increased tension in the blood-vessels, which lasts only a few minutes. This is equally true whether the animal is in a normal condition or has an acute peritonitis. The improvement in the arterial tension lasts somewhat longer when the **adrenalin** is given **with a saline transfusion** than it does when the adrenalin is given alone. Heineke (Zentralbl. f. Chir., S. 72, Beilage, 1909).

Tuberculous Peritonitis.—In theory the local focus of disease which has caused an extension of the process to the peritoneum should be excised, whether this is in the intestine, Fallopian tube, appendix, or other removable tissues. But this is not always practicable, and, furthermore, patients often recover under simple laparotomy and drainage. The author in a series of experiments with animals some years ago came to the conclusion that this cure of tuberculosis of the peritoneum after opening the peritoneal cavity was due to the presence of toxins developed from bacteria which grew in the culture medium of peritoneal exudate exposed by way of the drainage-tube. This was in fact true, and the cultures of tubercle bacilli in test-tubes were instantly killed by toxins extracted from such fluid and applied to the cultures. A later theory, however, and one

which is borne out by later studies, is that the tubercle bacilli are destroyed by phagocytes in the course of the intense hyperleucocytosis which promptly follows opening of the peritoneal cavity for any purpose. The idea that such hyperleucocytosis proves destructive to the tubercle bacilli is further substantiated by the fact that various substances injected into the peritoneal cavity have proved effective in the same way, and for the destruction of tubercle bacilli in the peritoneum it apparently matters little which method for exciting exaggerated hyperleucocytosis is chosen, so long as we bring about that phenomenon.

The onset of symptoms as shown by a study of 122 cases is often sudden and stormy, both in the cases where there is ascitic fluid present and where it is absent. Fluid can go quickly and improvement take place very rapidly both with and without an operation. Tuberculous peritonitis can be latent, unsuspected, so far as symptoms are concerned, and it can remain apparently unchanged for months after active symptoms have subsided and the patient returned to apparent health. Foci for the infection of the general peritoneum have not been found in the Fallopian tubes or in the vermiform appendix in this group of cases.

Operation should only be undertaken when there is some distress from the distention; it is better to wait for a period with the patient at rest and under the same hygienic conditions to which any case of pulmonary tuberculosis would naturally be subjected, namely, rest, fresh air, good food, and, later, moderate regulated exercise. If after six or eight weeks there is no improvement in the symptoms operation should be considered.

When once the disease is arrested, whether by operation or hygienic methods of treatment, the patients must be taught to regulate their lives with the same care that they would had their disease been located in the lungs. A. K. Stone (Boston Med. and Surg. Jour., May 7, 1908).

Ascites.—We speak of surgical treatment of ascites rather than of cirrhosis of the liver in cases of the latter disease, because the operation has probably little influence upon the liver itself. Ascites and hydroperitoneum from whatever cause may be relieved temporarily by paracentesis.

The incidental laparotomy with drainage corrects the condition for the time being. We have to be particularly careful to guard the peritoneum against infection in many of these cases, for the reason that the current of lymph is outward from the peritoneum, and it becomes exposed to various bacteria. When the current is inward, as in normal conditions, there is destruction of entering bacteria by the action of blood- and body- cells.

Study of the accidents which may follow paracentesis for ascites. These may be classed into five principal categories, viz.: serous anemia, icterus gravis, hemorrhages of the abdominal wall, hemorrhages of the digestive canal, and cardiac dilatation *a vacuo*. 1. In every case of cirrhosis the physician should rigidly insist on the proper diet and treatment and not waste time with half-measures. 2. In every case of puncture for ascites the condition of the heart should be investigated, and when indicated a preventive cardiac tonic treatment instituted. All the elements of prognosis should be weighed in each particular case. 3 A small trocar should be used, the dorsal decubitus should be maintained, and a very firm bandage should be placed about the body immediately and kept in place for a week or longer if the patient gets up. The place of election should be at the junction of the middle and outer thirds of the umbilicoiliac

line. 4. After the operation the patient should not be left, but should be closely watched in order to be able to institute in time any medication which may be necessitated by the occurrence of any of the above-mentioned accidents. Perrin (Presse méd., Sept. 23, 1908).

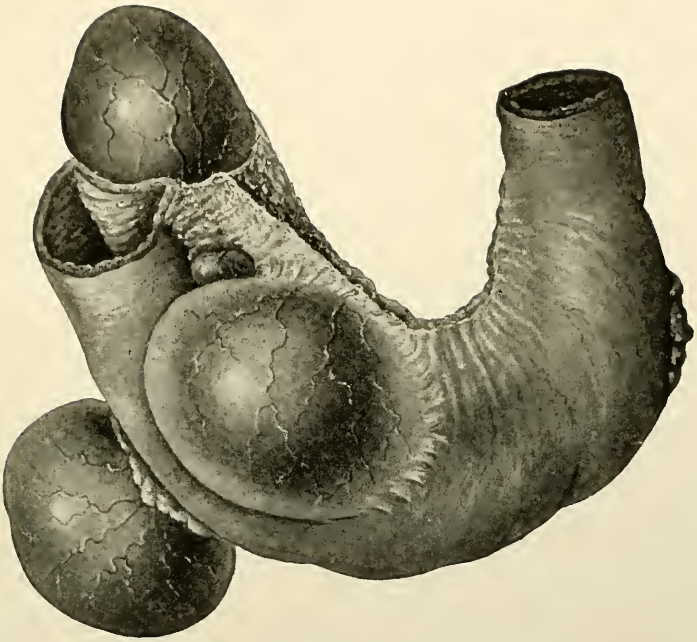
Omentopexy or the *Talma-Drummond operation* has for its aim the establishment of adhesions between the omentum and parietal peritoneum. These adhesions become filled with capillary blood-vessels in time, and the free network of small new vessels constitutes a venous anastomosis around the area of obstructed circulation. This work may be done by introducing numerous pinpoint sutures, or by pulling the omentum between the transversalis fascia and the posterior sheath of the rectus muscle, and fixing it there.

In addition to establishing a new circulation by the roundabout way of adhesions of the omentum, it is well to scarify the cephalad surface of the liver and the corresponding peritoneum of the diaphragm. This may be done very rapidly by the use of a nailbrush with the bristles cut very short. The peritoneum which has been denuded of its endothelium in this way throws out abundant lymph and makes extensive adhesions, which later are filled with new capillaries. The operation seldom accomplishes the object for which it is intended in a satisfactory way, because it is commonly used as a last resource when changes in the liver have become too far advanced. The operation performed before ascites has become a disturbing feature is sometimes distinctly of value, particularly when the omentum is fixed to structures extra to the peritoneum.

The more popular method is indirect anastomosis, which may be done either by sewing the omentum to the liver and diaphragm, by sewing the omentum to the skin of the abdominal wall, by fastening it between the outer layer of the peritoneum and the muscular part of the abdominal wall, or only to the surface of the parietal peritoneum. The two latter methods are employed most frequently. Drainage is unnecessary. Local anesthesia is often sufficient for the operation. Of 108 cases which the author has collected, 58 were improved or cured, 14 were not improved, and 36 died. The results in hypertrophic cirrhosis seem to have been somewhat better than in atrophic, 66 per cent. of the former recovering and only 45 per cent. of the latter. Turgard (Annales de la Polyclinique de Lille, Nos. 5 and 6, 1904).

Three cases of cirrhosis of the liver with ascites in which the writer made an exploratory laparotomy and twelve others in which he performed the Talma operation. Three of the patients in the latter group were restored to health. The results are better, the earlier the operation is done. None of the patients was permanently cured whose ascites was due to peritonitis rather than to the cirrhosis. Lieblein (Mitt. a. d. Grenz. d. Med. u. Chir., Bd. xviii, Nu. 5, 1908).

The benefit of the Talma operation for Banti's disease is due to the laparotomy and the resulting hyperemia rather than to the omentopexy. The latter helps, but the hyperemia from the laparotomy is the main factor, as determined in the course of 10 such cases. In operating the writer aims to induce hyperemia as much as possible and to remove all traces of the ascites. If the kidneys are functioning defectively, absorption of ascitic fluid left behind may prove fatal. He knows of two such deaths, and warns that pronounced kidney disease contraindicates the operation, and that in all cases the general anesthesia should be as slight as possible. Bogojawlensky (Zentralbl. f. Chir., Feb. 27, 1909).



Congenital Cysts of the Mesentery. (*H. C. Deaver.*)

Annals of Surgery.

Three cases in which the writer followed Ruotle's method of treating chronic ascites with cirrhosis of the liver by suturing the peripheral end of the saphenous vein, severed 8 cm. above its mouth, to the peritoneum just above Poupart's ligament. In the first case, a man of 38, the patient is well, with no return of ascites after the operation a year ago; in this case omentopexy, decapsulation of both kidneys, and continuous abdominal drainage had failed to cure. In the 2 other cases the ascites was the result of pericarditic pseudocirrhosis of the liver; here none of the operations done, including the Ruotle, gave relief. T. Soyesima (Deut. Zeit. f. Chir., April, 1909).

Surgery of the Mesentery and Omentum.—Aside from surgical affections which involve the mesentery along with the intestine, the former suffers from surgical affections peculiar to itself, more especially solid tumors and cysts in the omentum and mesenteric folds. They do not, as a rule, cause acute or complete ileus, but cause pressure symptoms, and if left alone tend to set up low-grade peritonitis and adhesions to neighboring viscera.

These growths should be extirpated whenever operable. Cysts with dense adhesions and chylous cysts can only be managed by drainage.

There are four ways of dealing with congenital intramesenteric cysts: (1) by aspiration; (2) by cystostomy and drainage, with or without the use of caustics; (3) by enucleation, and (4) by resection of the involved intestinal segment. The first method is obsolete, the second is useful in the presence of numerous adhesions, the third is ideal when practicable, and the fourth is the best in multiple juxtaposed cysts when too much surgical interference, as from dealing with cysts one by one, carries more risk than simple resection. Four personal cases. H. C. Deaver (Annals of Surg., May, 1909).

SURGICAL DISEASES OF THE INTESTINES.—Ileus.—Most of the conditions which require surgical intervention for the intestine, excepting traumatisms, are brought about by ileus or intestinal obstruction of some form. This is not the place to discuss the manifold agencies which produce obstruction, nor their recognition before operation. Once acute obstruction is evident, the surgeon is usually obliged to open the abdomen, his course afterward depending on the nature of the obstruction. In conditions like intussusception, volvulus, intestinal hernia, or obstruction adhesions, the obstructed loop is released, and steps described for the separate conditions are taken to prevent a recurrence of the trouble. If the mesentery is too long, or the intestine too mobile, a reef may be taken in the former, or the latter may be anchored to the abdominal wall or excised. If the intestine has become strangulated and is gangrenous, enterectomy is indicated with secondary anastomosis. If the obstruction is from foreign bodies, as with round-worms or gall-stones, for instance, the substance should be worked back to an empty portion of intestine, and an enterectomy or colectomy for foreign bodies performed. If the loop of intestine shows serious changes as a result of obstruction, a temporary artificial anus may be advisable. Excision is seldom required in such cases. In cases of acute ileus from any cause secondary peritonitis may develop and require treatment (see Peritonitis). While acute ileus may result from stricture or tumors, such conditions are much more apt to produce chronic stenosis, while ultimately if left alone will produce chronic ileus.

Such cases naturally tend to come to operation before ileus develops. Benign growths and cysts of the mesentery, and similar formations which do not compromise the integrity of the intestine may be removed without much interference with the latter. Tumors of the gut itself necessitate excision of the latter with secondary anastomosis, or establishment of artificial anus. Tuberculous strictures are treated by enteroclusion, or enterostomy for drainage, excision being, as a rule, contraindicated. The same is the alternative in inoperable carcinoma.

Volvulus.—Volvulus most often occurs in the pelvic colon, and consequently does not belong to this group of articles, but it may occur in the sigmoid or cecal region. In the latter case, after untwisting the volvulus and separating any peritoneal adhesions, a rectal tube should be passed and the poisonous contents of the volvulus massaged gently but rapidly toward the rectum, provided that no gangrene of the volvulus be present. The prevention of recurrence by approximation to the anterior abdominal wall by Roser's method is uncertain, and the author favors complete excision of the part of the bowel engaged in volvulus, as this can readily enough be spared, and an end-to-end or lateral anastomosis of the remaining segment of bowel fulfills the indication. Volvulus of the cecal region occurs when there is a congenital form of defect giving a sort of mesocecum which may be quite long. Excision of the cecum and intestinal anastomosis are preferable to any attempt at preventing the recurrence of twisting of the cecum.

Volvulus of the small intestine occurs most frequently when the coil of bowel is caught by an adhesion band, and peristaltic progress may loop the bowel in such a way as to cause torsion.

> To test the viability of strangulated intestine the writer proceeds as follows: He relieves the constriction at the neck of the sac and reduces the affected part of the intestine into the abdominal cavity, but he retains a portion of adjacent and contiguous intestine in the wound so as to be able to withdraw and inspect the suspected loop. After from three to five minutes after reduction he again inspects the loop. All traction on the mesentery is thus avoided, and the intestine is kept warm and moist in its natural habitat. Infection of the hernial sac or advanced impairment of circulation with beginning gangrene contraindicates this method. S. C. Plummer (Surg., Gynec., and Obstet., June, 1911).

Localized paralysis of the bowel occurring in typhoid fever may lead to this twisting of the bowel upon itself, and the twisted part can best be excised if the patient's condition allows it.

Intussusception.—In a child with the patient under an anesthetic, an intussusception can sometimes be reduced by the hands on the abdomen, but the last inch is very difficult of reduction, and we are likely to do damage by persistent efforts. There is the same objection to water injection, as we cannot know whether the last inch has been reduced or not. Furthermore it is very easy to rupture the bowel of a child. We may reduce an intussusception better through a very short incision, even though children bear the operation so badly. Perhaps it is best not to apply many of the resources for intussusception described in the older text-

books, with the exception of operation by immediate laparotomy. There is no occasion in this article to describe the many varieties of intussusception, because the principles of treatment are practically the same in all. Reduction of intussusception is so likely to be followed by recurrence that operation is an addition that is preferable in many cases. The part of the bowel engaged in intussusception is of no value, and consequently excision of the bowel with anastomosis is in order, unless the patient is in a desperate condition, in which case we may simply approximate any two loops of bowel above or below the intussusception and unite these in the common way with a Lembert suture.

Intussusception cannot progress beyond the point at which such anastomosis has been made.

In emergency cases of intussusception, with the patient *in extremis,* the author likes the method of making a quick lateral anastomosis immediately above and below the area involved in the intussusception. If two traction sutures are used for approximating the loops of bowel to be anastomosed the work can be done very quickly and with little traumatism.

The results of this procedure in emergency cases would seem almost to justify the simple resource as a regular procedure. Intussusception cannot progress beyond the sutured area. The invaginated part of the bowel in the intussusception may slough or undergo subsequent atrophic changes without adding a serious feature.

Typhlitis.—Not readily distinguishable from appendicitis, and is usually treated by simple opening of the abscess and drainage.

Meckel's Diverticulum.—One of the remains of the vitelline duct is sometimes attached to the convex border of the intestine, and varies considerably in range, as well as in character. In some cases it closely resembles the part of bowel from which it springs. Consequently all varieties call for their respective forms of treatment.

Sometimes the entire tube remains as an opening at the umbilicus, but more commonly we have only the patent part of the tube near the bowel with a cord-like remainder extending to the umbilicus. Foreign bodies may escape into this diverticulum, or ordinary intestinal contents may result in exciting inflammation. Adhesions may produce angulation of the tube, interfering with circulation and leading to infection. Sometimes the diverticulum acts as a constricting band in intestinal obstruction, in which case it takes part in acute inflammatory process and may become gangrenous. Volvulus of the diverticulum may occur.

Diverticula of the colon may occur at any point, and often consist of anatomic defects opening into epiploic appendages. Increased pressure within the bowel at any time may lead to considerable enlargement of one or more such diverticula, and later with obstruction and inflammation.

Epiploic appendages when twisted upon their long axes may become congested and even gangrenous in very fleshy patients, but the treatment is simply for abscess which follows.

Diverticulitis of the sigmoid region is the most common, giving symptoms quite similar to those of appendicitis, excepting for location of tender-

ness. The infiltrated tissues may respond to external applications of heat or cold, but frequently we must operate for the abscess which remains.

Wounds, Perforation from Within, etc.—In cases of solution of continuity in the intestine, whether from penetrating wounds from without or perforation from ulcers within, the course of procedure is the same. Laparotomy is performed and the wound or perforation sutured, unless the wounds are multiple and so close together that suture would cause too great a reduction of caliber, in which case an anastomosis may be necessary. In one case of lacerated and contused ileum, the author quickly covered perforations with cargile membrane without suturing. The patient recovered without fistula. If large blood-vessels have been wounded they must be ligated. In all these cases it is necessary to carefully cleanse the peritoneal cavity in the vicinity. The question of subsequent drainage depends on the individual case and the surgeon's point of view.

TYPICAL OPERATIONS OF THE INTESTINE.—Enterorrhaphy.—This term is applied to suture of the intestine for wounds or ulcers which are not extensive enough to require excision and anastomosis. The chief amount of intervention is in connection with the external incisions and examination of the intestine to determine the extent of the injury, which may involve more than the bowel itself. Hemostasis and cleansing of the peritoneal cavity will necessarily be required in traumatism from without, as well as in perforating ulcer from within. It will often be necessary to incise the mesentery in order to complete the examination, and these incisions must always be sutured in such a way as to leave no point uncovered by peritoneum.

Perforation may, as a rule, be sutured without preliminary excision of tissue. The suture should run parallel with the long diameter save when the traumatism is near the pylorus. In this locality it should be applied in the transverse diameter. It is exceptional for an external traumatism to consist only of a single perforation of the intestine, for, as a rule, not only is the bowel itself penetrated doubly, but other portions of intestine and mesentery are involved in the knife or bullet wound. Hence single isolated trauma occurs most naturally from the internal perforations.

Multiple perforations of the bowel and mesentery are adaptable for suture, no matter how numerous, if they are not too close together; but, when a portion of bowel is, so to speak, riddled by bullet or other wounds, it should be excised, unless the author's resource in one case quoted above introduces a principle in addition.

For suturing perforations a few points of interrupted Lembert silk or linen suture are usually sufficient. In multiple perforation or when there is suspicion of such, it is advisable to suture as soon as the wound is located, and before proceeding with further examination.

The rule for determining the possible limit of suture in contrast to excision is this: if the suture of one or more openings does not diminish the caliber of the intestine by more than a third, suture is indicated in place of excision.

In perforation from typhoid ulcer

multiple traumatism is unusual, and the lesion in most cases is seated not far from the ileocecal valve. Owing to the general state of the patient the operation must be rapidly done, as a rule. An appendicitis incision usually suffices.

The perforation is closed at once by a few interrupted sutures, or a purse-string suture. Cases of typhoid perforation do occur in which, either from the size, number or complications of the lesion, enterostomy or enterectomy is required, but the condition of the patient sometimes makes it desirable to quickly fasten the bowel opening near to the external opening, and to do a secondary excision operation after recovery from the typhoid. The friable character of tissues distended with serous infiltrates also makes this expediency work necessary when the friable tissues refuse to bend freely to sutures. Even after simple suture it may not be advisable to close the abdominal wound, in contradistinction to the course pursued in suture of external wounds. The presence of peritonitis with adhesions may make it advantageous to leave the lower angle of the wound open for the purpose of a little drainage.

> Review of the literature of intestinal perforation in typhoid fever showed that those operated upon in which perforation was found consisted of 269 cases (from 1903 to 1909); 156 of this number resulted fatally, giving a mortality of 57.99 per cent., while Harte and Ashhurst (all cases from 1884 to 1903), in a similar study, found 311 cases, with a mortality of 73.31 per cent. While it is true that in the number of cases reported during the previous twenty years the proportion should be much greater, when we consider the rapid strides in other abdominal operations during this period, it is also true that the mortality shows improvement, but certainly this improvement is not as great as has been accomplished in other surgical conditions. During the period 1903-1909 nothing new has been developed which will aid in the diagnosis, and, while a great deal has been said about treatment, very little real value has been added to the treatment. Charles Bagley, Jr. (Surg., Gynec., and Obstet., Aug., 1911).
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> In a search through the literature since 1903, the writer found 133 reported cases of typhoid fever in which perforation occurred and was closed by suture. Of this number 68.5 per cent. died and 31.5 per cent. recovered. When we compare the percentage of recoveries with the figures of Harte and Ashhurst's 25.97 per cent., made in 1904, and Platt's 20.3 per cent., made in 1899, and Keen's 19.36 per cent., made in 1898, and Fitz's 10 per cent., made in 1891, we cannot help but conclude that real progress is being made in dealing with this heretofore-fatal complication of typhoid fever. Combining his own 133 cases with the 362 collected by Harte and Ashhurst, we have a grand total of 495 cases, of which 27.4 per cent. recovered and 72.53 per cent. died. These figures probably express fairly accurately the results of the surgical treatment of perforation in typhoid at the present time. G. D. Head (Jour. Minn. State Med. Assoc., Aug. 1, 1911).

Enterectomy.—Excision of portions of intestine is performed for a great variety of conditions, such as traumatism, malignant tumors, actual or impending gangrene, etc. It is indicated, therefore, as an operation of choice or necessity in many of the conditions which constitute or give rise to ileus. The part to be removed may vary in length from two or three inches to a number of feet. In enterectomy, as in similar operations, the actual operation requires much less time and a much simpler technique

than the secondary stage of restoring the continuity of the intestine. There is in fact but one technique for the former, while the latter is not only practicable by quite different operations, but each operation may be performed by a number of different methods.

For the performance of the enterectomy proper, it is necessary to excise a portion of intestine with a certain amount of mesentery. After the external incisions and exploration of the abdomen the portion of intestine to be excised is, if necessary, freed from adhesions. This coil of intestine should be milked into the portions of the gut continuous, for which purpose the fingers of assistants must be used. After one-half of the coil is thus emptied in one direction the fingers should compress the gut to prevent re-entrance of intestinal contents; the other extremity is then similarly treated. Instead of the fingers of assistants, clamps may be applied, one at either end and some inches beyond the segment of gut to be excised. Loops of gauze may also be used, but in such a case the mesentery must be penetrated, and it is best to use the fingers of assistants as far as possible.

Before excising, the mesentery must be ligated off close to the intestine,—about one inch distance. An approximate rule is to place a catgut ligature for every inch of mesentery. Another is to ligate less rather than more mesentery than is apparently called for. This is done on the principle of overcorrection, because if too much mesentery is sacrificed the edges of the anastomosis to be performed may suffer gangrene from interference with blood-supply.

When all preliminaries have been completed the gut with its mesenteric stump is removed by means of the scissors.

Series of 22 cases in which from 192 to 520 cm. of the small intestine were resected for various reasons. The patients did not seem to be incommoded by the loss of such a stretch of intestine, and all were in good health at last accounts, except for a tendency to diarrhea in a few cases and the death of one patient three weeks after removal of cancer with metastases. In a personal case described, on account of sarcoma of the root of the mesentery, the author removed the entire ileum and part of the jejunum, a total resection of 510 cm., or 17 feet, of the small intestine. The patient gained twelve pounds in three months, with normal stools, but the malignant disease recurred after five months, and the patient, a blacksmith of 21, was dismissed as incurable. No metastases were detected at the primary operation. The good functional results in these cases justify resection of two-thirds or even more of the small intestine when required. Storp (Deut. Zeit. f. Chir., Bd. lxxxvii, Nu. 4-6, 1907).

Research on dogs and pigs, showing the late effects on the animals of various operations on the large intestine. The animals all became emaciated or died after unilateral subtotal exclusion or resection of the large intestine with ileosigmoidostomy. On the other hand, the animals bore without apparent injury resection of the ileocecal segment. Simple ileosigmoid anastomosis also proved harmless for dogs and pigs, both at the time and months later. Simple ileosigmoid anastomosis, however, always proved fatal for herbivorous animals, as also exclusion of the large intestine. Total exclusion of the large intestine, with an anus at the end of the small intestine, always entailed the death of the dogs in ten days and of the pigs in thirty—sooner than in death from starvation. Alglave (Revue de Gynéc., Pozzi's, vol. xi, No. 1, 1907).

In 5 personal cases of resection of the small intestine for gangrene the length removed varied from one foot five and a half inches to nine feet six inches. Four patients recovered, none being under 50 years of age; the oldest was 65 years. The recoveries were smooth, without high temperature. Three of the patients did well subsequently; the fourth, a woman, 59 years of age, from whom nine and a half feet of intestine were removed, succumbed to a steadily progressing marasmus after seven months, showing that at that age the removal of half the small intestine is unsafe. Whatever the length of resected intestine might be, the anastomosis must be in absolutely healthy tissue. Lateral anastomosis should be the rule whenever practicable. The cases were all emergency cases of gangrenous herniæ. Childe (Practitioner, March, 1909).

There have been reported since 1906 but three or four successful cases of enterectomy in children under 1 year. The authors' case was a female infant, aged 7 months, with irreducible intussusception; temperature, 100°; pulse, 164; respirations, 36. A resection of the bowel was made, including the cecum, appendix, and a part of the colon. The operation was successfully performed under spinal anesthesia, using Gray's stovaine, dextrin, and saline solution. A second injection of stovaine was given just before anastomosis was made, as the patient was beginning to show signs of shock—the effects of the first injection having begun to wear off. The authors believe that the spinal anesthesia saved the child's life, while chloroform anesthesia would have proved fatal. The child received three pints of **saline solution** daily by the rectum and subcutaneously for five days before nourishment was begun, with small doses of **morphine.** Spinal anesthesia cases show practically no shock. The Murphy button used in the operation passed in eighty-two hours. Fairbank and Vickers (Lancet, Feb. 5, 1910).

Rapid resection of the gut may be performed by dropping half a Murphy button in each end of the gut; tying up the ends of the gut with fine silk ligatures, and disinfecting them with carbolic acid; pushing the halves of the button together to complete the anastomosis; closing the V of the mesentery with a stitch; and finally, drawing the wound together with a silkworm-gut suture. In respect to the after-treatment, water is given at once, and the stomach washed out with a tube, as required. After twenty-four hours, albumin water and beef-juice are given, and after forty-eight hours malted milk. No laxatives or hard foods are given for a week. The bowels are moved in three or four days by enemata or suppositories.

This combination of methods is suitable for any case demanding resection of the small intestine, and is especially useful if great haste is required. It may be done under local anesthesia, especially if morphine and hyoscine are used. W. L. Wallace (Amer. Jour. of Surg., Feb., 1911).

Enteroanastomoses.—These methods of restoring continuity of the intestine after enterectomy comprise three distinct types. The first and most natural is end-to-end anastomosis or suture, which in most cases is the operation to choose.

The second type is known as the side-to-side laterolateral or simply lateral. It differs in scope from the preceding chiefly because it may be used between the small and large intestines, and small intestines and stomach.

The third type is known as end-to-side or terminolateral, or simply as the implantation method. It is restricted in practice to implantation of a cut end of small intestine into the stomach or colon. The first-named has already been considered in part under pylorectomy. The latter is specifically known as ileocolostomy, or ileosigmoidostomy.

Gastroenterostomy. — This operation consists of a lateral anastomosis between the stomach and some portion of the small intestine, either the duodenum or jejunum. According as the intestine is united to the anterior or posterior stomach wall the operation is known as anterior or posterior gastroenterostomy.

The operation is indicated in certain cases of gastric or duodenal ulcer, either as a primary resource or one secondary to pylorectomy or gastrorrhaphy. Generally speaking the operation is one of necessity when milder measures have failed or are likely to fail. Minor indications for gastroenterostomy are found in contraction of the pylorus from swallowing corrosive poison, in congenital hypertrophic stenosis of the pylorus, and finally in certain cases of cancer in this locality, as a palliative when pylorectomy cannot be performed.

Roentgen-ray pictures taken before the operation and soon after and again after an interval of a year or so in 22 cases. They showed that the stomach evacuation proceeded after a gastroenterostomy not merely by the laws of gravity, but by a kind of physiologic sphincter process. The cases teach further that when the new opening is made on account of anatomic stenosis it answers the desired purpose completely from the practical point of view. When the stenosis was merely spastic the gastroenterostomy overcomes the tendency to contraction and the pylorus becomes permeable once more. Conversely, an ulcer in the middle part of the stomach is not much influenced by the gastroenterostomy; most of the food still passes out through the pylorus instead of through the new opening. One or more internal courses of treatment for the ulcer should follow every gastroenterostomy. Härtel (Deut. Zeit. f. Chir., April, 1911).

Examination of 40 patients to ascertain present conditions after a gastroenterostomy, and analysis of the findings in 25, including 13 cases in which the pylorus was resected. The findings taught the necessity of making the opening at the lowest point of the stomach after resection, and also that the gastric digestion nearly always suffers after a gastroenterostomy. Schüller (Mitteil. a. d. Grenz. der Med. u. Chir., Bd. xxii, Nu. 5, 1911).

The operation is contraindicated in so-called medical diseases of the stomach, however severe these may be.

The ideal operation is one in which the opening is made as nearly as we can to the pylorus and the proximal loop of jejunum, thus utilizing the part of the stomach which is commonly the lowest during the process of digestion. This will allow free regurgitation to the alkaline intestinal juices. Anastomosis with the cardiac part of the stomach would allow acid contents to escape in case of good digestion, and defect of pyloric digestion would be the result. In addition, cases have been reported in which jejunal ulcer has followed the forming of an opening at a point where acid contents could injure the tissues. The choice of procedure in gastroenterostomy at the present time is probably the so-called posterior no-loop operation, and the author has referred to older operations which are necessary at times. Even with ulcer of the stomach in the cardiac end of the stomach, the posterior no-loop operation should be made with the pylorus, if possible, to avoid the effects of gastric acidity at some distant point from the pylorus. The posterior no-loop operation is performed by making an opening

through the transverse mesocolon in the usual way, avoiding the middle colic vessels. The posterior surface of the stomach being exposed, a portion near the pylorus part is chosen and drawn through the opening. The jejunal flexure close to the duodenum is found beneath the left of the mesocolon, and the proximal loop is employed for completing the gastroenterostomy, but in such a way that when the parts are released from the fingers or clamps the intestine will hang in a direction which is almost vertical, but with a slight inclination toward the left or right, in a normal line of the long axis of the individual jejunum. This is the essential part of the posterior no-loop operation.

Conclusions based on 214 gastroenterostomies. The operation gives the best results in cases in which there is organic disease in the prepyloric or pyloric regions of the stomach or duodenum, or when performed on the cardiac side of a stenosis in the body of the stomach. When an ulcer is found on the lesser curvature near the cardia it should be excised, if possible; gastroenterostomy is not necessary, and if performed is either almost useless or entirely harmful. When there is a suspicion of malignancy in an ulcer or ulcers in the pyloric region, Rodman's operation should be performed. Under no circumstances, and in compliance with no persuasion, however insistent, is gastroenterostomy to be done in the absence of demonstrable organic disease. Regurgitant vomiting, formerly the most troublesome of all complications, is dependent on faults in the operation which result in some mechanical obstruction to the intestine. These faults are chiefly dependent on the presence of a loop in the jejunum, but may also be caused by a twist in the intestine around its longitudinal axis at the time of its application to the stomach. The posterior no-loop operation with the vertical application of the bowel to the stomach is the best procedure. Moynihan (Brit. Med. Jour., May 9, 1908).

If the edges of the cut mesocolon are fastened to the stomach wall before completing this gastroenterostomy, it will obliterate the opening in the mesocolon, and this is desirable for avoiding subsequent hernia, if the patient's condition allows us to follow ideal technique. When adhesions or extensive scarring or other mechanical reasons make the posterior no-loop operation of gastrojejunostomy difficult, we may use gastroduodenostomy instead. The anterior wall of the pylorus is joined with the descending part of the duodenum, but where we suture the mesocolon to the stomach it avoids the danger of subsequent hernia.

The most frequent source of bad results after gastroenterostomy is a position of the fistula causing the food to enter that part of the bowel which leads back to the stomach. To avoid this the loop of the intestine selected must be as close as possible to the stomach, and not the first loop that comes to hand; again, it should always be sewed antiperistaltic. Finally, the opening in the stomach must not be larger than the lumen of the loop of bowel. If these rules are followed there will probably be no trouble. Delaloye (Deut. Zeit. f. Chir., Bd. lxxxiii, Nu. 6, 1906).

Report of 3 cases of gastrojejunal and jejunal ulceration following gastroenterostomy. There was a recurrence of gastric symptoms, in 1 case a few weeks after the gastroenterostomy, in the others two years after. In accord with the observations of others, the author concludes as follows:—

1. Two types of jejunal ulceration must be distinguished, the one—gastrojejunal—in which the ulceration occurs at the site of the anastomosis; the other —true jejunal ulceration—in which one

or more ulcers form in the jejunum at some distance from the anastomotic opening. 2. In the great majority of cases the ulceration has occurred at or close to the gastrojejunal anastomosis. 3. The ulceration may manifest itself at any period after the gastroenterostomy operation, from a few weeks to several years. 4. The formation of the ulcer is usually associated with a recurrence of the gastric symptoms, but in some cases symptoms of perforation have been the first evidence of the ulceration. 5. The tendency to perforation is apparently greater than in the case of gastric ulcer, and the death rate from such perforation is high. 6. In all the recorded cases the preceding gastroenterostomy has been carried out for the relief of a *non-malignant* affection of the stomach or duodenum (Key has recorded 1 case as jejunal ulcer after gastroenterostomy for gastric carcinoma, but the evidence is unconvincing). 7. Jejunal ulceration has been met with after every variety of gastroenterostomy, but it occurs probably more frequently after an *en Y* type of anastomosis than after the simpler forms of operation. 8. In the majority of cases the preceding gastric lesion had been associated with hyperacidity, but in not a few cases there had been no excess of free acid. 9. The jejunal ulceration is probably caused by the action of the acid gastric juice on the jejunal mucosa, which, under normal conditions, is exposed to an alkaline medium. T. P. D. Wilkie (Edinburgh Med. Jour., Oct., 1910).

Analysis of 48 cases of gastroenterostomy for ulcer of the stomach. There were 15 deaths, in 1 of which the patient, after an uneventful progress for fifteen days after operation, succumbed to peritonitis induced by a gangrenous appendix, the site of operation not being affected. The case is an argument in favor of appendicectomy with every gastroenterostomy. In 2 other cases death was due to carcinoma after apparent recovery. In the majority of patients who died, surgical treatment should have been resorted to earlier, as shown by the advanced degree of stenosis shown at operation. In 21 of the 48 cases there was ulcer of the stomach or duodenum with stenosis, and 14 of these patients recovered perfectly, and only 1 was unimproved. There were 3 patients operated on with ulcer without stenosis; 1 recovered, 1 has improved, and 1 remains unimproved. J. D. Dunham (Jour. Amer. Med. Assoc., Nov. 19, 1910).

First instance in the human being where the proposed fistuloenterostomy of von Subenrauch was carried out successfully. This procedure uses a diverted segment of intestine as a canal to carry the discharge from a biliary fistula back into the intestinal tract. Sutton (Annals of Surg., Sept., 1910).

Experimental research by the writer confirming the view that peptic ulcers after gastroenterostomy are due to the action of the acid gastric juice on the intestinal mucosa, and that this acidity should be neutralized with alkalies in prophylaxis. After a gastroenterostomy the patient should keep up an ulcer diet for a long time. The author's experience indicates that the posterior retrocolic gastroenterostomy according to von Hacker, as near to the duodenum as possible, is the operation that is least liable to be followed by a peptic ulcer. Exalto (Mitteil. a. d. Grenz. der Med. u. Chir., Bd. xxiii, Nu. 1, 1911).

Anterior Gastroenterostomy.—This, the original procedure, has been replaced in most cases by the posterior operation, but is still performed when the posterior wall is unaccessible by reason of adhesions or organic disease. A fairly good rule is for the surgeon to do whichever operation he can do most easily in any given case, but the anterior operation gives more postoperative complications. The operation is as follows:—

After the stomach has been fully exposed, its anterior wall is so grasped that the fold which is to be the seat of the anastomosis runs

obliquely across from right to left, and from below upward. The intestine is similarly grasped about eighteen inches below the duodenojejunal junction and the two structures placed side by side.

The anastomosis is then carried out as in all similar procedures, one-half the outer plane of sutures being inserted before the incision is made. Details of technique may be considered under the posterior operation.

Posterior Gastroenterostomy.—The external incision is that used for other operations on the lower portion of the stomach and the pylorus, passing through the right rectus by blunt dissection, the posterior sheath and peritoneum being divided together. The incision is largely an exploratory one, for despite the evidence of a pyloric ulcer, for example, the entire stomach and duodenum with the neighboring viscera must be examined for complications and possible contraindications. The jejunum must also be examined with especial reference to its relations with other organs. The natural direction should be learned, for this may be to the right, left, or directly downward, and in bringing the intestine in contact with the posterior wall the original direction must be conserved.

> The results of different methods of posterior gastroenterostomy show that there is no "natural direction" of the jejunum, and consequently no "best line" for anastomosis. One is as good as another, provided no twist be given to the gut at the time of anastomosis. The main point is to choose for the anastomosis that part of the jejunum which is close to the flexure. This line can be directly approximated to the stomach without the gut being revolved on its longitudinal axis. Moynihan (Annals of Surg., April, 1908).

In order to gain access to the posterior wall it is necessary to go through the transverse mesocolon, the incision being ample enough to enable the posterior wall to be drawn outward; but the incision in the mesocolon, to avoid opening large blood-vessels, should be first made small, and then enlarged by stretching with the fingers.

Generally speaking the portion of this wall to be selected for anastomosis is at the lowest point of the organ, which is considerably nearer to the pylorus than to the cardia and fundus. The author likes to cut through the ligament of Treitz when approaching the posterior stomach wall. This brings one to a convenient part of the jejenum for the no-loop operation. He prefers traction sutures rather than instruments for approximating stomach and ileum during operative procedure. The portion to be incised for the anastomosis is pinched up in a direction corresponding to the natural direction of the jejunum itself. The latter is also grasped an inch or two below the duodenojejunal junction. As in all such anastomoses, a portion of the outer plane of sutures is introduced before the incisions are made. This is a continuous seromuscular suture, intended to fix the two structures together and furnish a guide to the incisions. The latter, some three inches in length, are not simple linear incisions, but a small spindle-shaped portion of tissue is excised. The two openings thus made are now sutured together by through-and-through stitches of the penetrating type, the two posterior margins being first united, and then the anterior margins, the inner layer of sutures being thus completed.

The fingers or clamps are removed, and the outer plane of serous sutures completed.

> In performing the posterior operation the writer advises that the operator locate the peritoneal suspensory ligament or band which extends from the transverse mesocolon to the upper part of the jejunum. Immediately above this band, in the mesocolon, is an area in which there are no important blood-vessels. The suspensory band having been stripped away, and a transverse incision made in the above-mentioned area of the mesocolon, the posterior aspect of the stomach may be drawn through this opening and the denuded jejunum attached to it, the attachment thus being without strain or loop and following the normal direction of the jejunum. Mayo (Annals of Surg., Jan., 1908).

Roux's Operation.—The Y-operation of Roux differs notably from the typical procedures just enumerated, being a combination of the anastomoses, both being examples of implantation of terminolateral anastomoses. The jejunum having been divided across, the peripheral segment is implanted into the posterior surface of the stomach, while the proximal segment is implanted into the jejunum.

It is no longer held desirable to use mechanical devices in most gastroenterostomies, although such aids were of great importance at one time in giving us confidence to advance to a simpler technique.

Gastroenterostomy is liable to be succeeded by certain typical complications. Among these are hemorrhages, sometimes inexplicable, but now generally believed to be due frequently to overlooked ulcers, or to imperfect suturing, or to the use of too-fine suture material which cuts out when the patient vomits. In bleeding ulcer of the stomach it is sometimes extremely difficult to recognize all of the bleeding surface while the tissues are held in tension. Relaxation of tissues and pressure on the viscera with the fingers or with gauze may start a free bleeding which localizes the ulcerated area. Post-operative ileus may develop, which may be due to obstruction from adhesions, to internal strangulation, or to angulation of bowel, particularly in the anterior operation, if the loop is not supported by side sutures in the omentum.

Aside from vomiting, which is symptomatic of this obstruction, we may have a non-obstructive type which supervenes at a late period (one or two months following operation). The nature of the vomiting is not always clear, but, since operators have sought to preserve the natural direction of the jejunum, cases of obstruction and vomiting have been much less frequent.

> The gastroenterostomies done at Kocher's clinic since 1898 amounted to 137, of which 92 were for non-malignant affections. All the patients have gained considerably in weight, except the 10 last operated on. The tendency to vomit also passed away, except in one patient, who vomits during the menses, and another patient, with nervous complications. The motor functions of the stomach return to normal in a surprising degree; the hydrochloric acid is generally reduced. After the operation the intestinal functions also returned to normal, as a rule, even in the cases of old, chronic, obstinate constipation. Pre-existing dilatation of the stomach generally subsided if of the second or third degree, but that of the first degree did not seem to be influenced by the operation. In 12 cases in which the gastroenterostomy was done for

carcinoma, the patients survived on an average nearly eight months. Gilli (Mitt. a. d. Grenz. d. Med. u. Chir., Bd. xviii, Nu. 1, 1907).

A complication of considerable gravity is peptic ulcer of the jejunum, attributed once to the action of digestive enzymes, but now regarded as having a common origin with ordinary gastric and duodenal ulcer, viz., hyperacidity (hyperchlorhydria) and toxic injury of terminal arteries. To lessen the frequency of this complication it is advisable that every patient to be operated upon be first treated for hyperchlorhydria. Peptic ulcers of the jejunum run a similar course to that of ulcers higher up, terminating at times in perforation.

At Feurer's clinic at St. Gallen, there have been 117 cases of gastroenterostomy. The use of this operation for cancer is growing constantly less, as the conditions are much better after resection of the pylorus. The mortality after resection has been only 16.66 per cent. of 42 cases, and zero in the last series of 20, while that of the gastroenterostomies was 25.64 per cent. Delaloye (Deut. Zeit. f. Chir., Bd. lxxxiii, Nu. 5-6, 1907).

At Hochenegg's clinic at Vienna, there were 56 cases of gastroenterostomy in which a sufficient interval has elapsed since the operation to judge of the permanent results. In 64 per cent. the patients had been entirely and in 24 per cent. almost entirely relieved of all disturbances by the intervention. The operation not only put an end to the disturbances from the stenosis, but was followed by the healing of the ulcer. Schulz (Deut. Zeit. f. Chir., June, 1907).

Report of 230 operations on the stomach, 112 of which were for malignant disease, from Schloffer's clinic at Innsbruck. In 82.6 per cent. of the 74 cases in which gastroenterostomy was done for a non-malignant affection, the patients were permanently cured (46) or materially improved (11). Of the 16 patients with cancer treated by resection, 4 are still living, 1 after three and a half years; the average survival was from two to nearly three years. Of the 69 cancer gastroenterostomies, 4 patients are still living, over a year since the operation. Kindl (Beiträge z. klin. Chir., May, 1909).

Condition of the patient one year or more after gastroenterostomy in 175 cases, 150 benign, 25 malignant:—

Benign Cases (150).—The immediate mortality (death within thirty-five days) was 10 per cent. Eighteen died within the first year (12 per cent.); 22 died of their gastric disorder within five years (14.6 per cent.). Six patients are alive, but have been operated upon within one year.

Of the 126 patients who survived the operation, and have been under observation for one year or more, 81 (or nearly two-thirds) were reported as entirely recovered, or well; 8 as much better, and 31 (nearly 1 in 4) as little or no better. Of the 150 patients, 89, or 60 per cent., were much better or entirely well; fully 30 per cent. died or were little or no better at the time of report.

Twenty-five cancer cases are reported, 20 being in men. Ten patients died within one month of the operation, an immediate mortality of 40 per cent. One is still living, two years after operation, another six months, and another four months. Ten patients lived more than four months after operation. Six of these were temporarily much improved, and gains of weight ranging from eighteen to forty-seven pounds are recorded. Two patients received no benefit at all from the operation. Bettmann and White (Med. Record, Oct. 9, 1909).

Results of Roentgen examination of 40 patients from a few months to six years after gastroenterostomy to determine its ultimate action. The author found that the stomach emptied itself in from ten to twenty-five minutes in 9 cases, in from twenty to fifty minutes in 15, and in about ninety minutes in 15. The gastroenterostomy thus answered

its purpose of rapid draining away the contents of the stomach in nearly every case, and this effect was obtained whether the pylorus had previously been permeable or not. A. Pers (Ugeskrift for Laeger, Sept. 30, 1909).

A male baby, aged 6 weeks, was submitted to gastroenterostomy for congenital stenosis of the pylorus. At the age of 5½ months the baby weighed 12 pounds 12 ounces, having gained 4 pounds since operation. The figures indicate that the digestion and absorption of the fat and nitrogen were normal in this baby three and one-half months after the operation, and they are evidence that the operation of gastroenterostomy does not change the powers of digestion of these two food components and agree with the results published by the writer in earlier investigations. Talbot (Boston Med. and Surg. Jour., April 14, 1910).

Fatal postoperative diarrhea sometimes occurs. Its nature is obscure and seems to depend upon derangement of bowel function due to shock to the sympathetic ganglia.

End-to-end Anastomosis after Enterectomy.—This may be effected by suture, or Murphy's button. The suture methods in use comprise the simple direct suture, the combination of suture and invagination, the Connell method, etc.

Simple Suture.—The mesentery is first united by transfixing both the cut edge of the gut just beside the mesentery, and then the latter close to its insertion. The same through-and-through suture is then passed in the reverse order through the opposite mesentery and gut. A duplicate suture is now passed through the other side, or the same suture may have its other end threaded in a needle and be used for this purpose. When this suture is tightened the gap in the mesentery is closed with approximation of the cut ends. The remaining step is suture of the latter, and this may be done by carrying the original two-tailed mesenteric suture from its knot around the circumference of the gut on either side until most of the circumference has been sutured. The opening which remains is closed with an outside Lembert suture. The rent in the mesentery is closed with a few points of catgut.

Maunsell's Method.—The divided surfaces of intestine are placed in rough apposition by four traction sutures at equidistant points, the first at the mesenteric insertion. The next step is to introduce a pair of forceps through the intestinal wall from without inward, and to this end a slit is made in the long diameter of the bowel, one (either side) segment opposite the mesenteric insertion and about one and one-half inches from the cut edge. With this forceps the loose ends of the traction sutures, previously twisted together, are tightened with production of an invagination of the distal into the proximate segment, the two serous coats being in contact. In this position the two edges are united with a chromicized-gut suture applied through-and-through, the traction sutures are removed, and the invaginated segment replaced. An external durable Lembert suture is now applied.

Connell Method.—As in the preceding operation, four traction sutures are applied, and the two cut edges of intestine are sutured, one-fourth at a time. The traction sutures which limit each quadrant are tightened in turn, and the intervening intestine joined by applying a right-angled through-and-through suture. As soon

as a portion of the gut is reunited one of the tractors becomes unnecessary and is removed. At the close of the suturing the two free ends are threaded within the lumen of the intestine upon a ligature carrier, brought outside and tied, and the knot is then worked back on the inside of the gut.

Murphy Button.—Purse-string sutures are applied at either divided segment and tightened upon the halves of the button. The suture for each side is a two-tailed one, and first transfixes the mesentery at its insertion. The tails are then carried down on either aspect of the intestinal segment to the point opposite the mesenteric insertion, the suture of chromicized gut being applied overhand. The two tails of the suture having been tightened upon the halves of the button, these are then joined and locked. The rent in the mesentery is now repaired and an outside durable Lembert suture applied over the inside suture. Great care is taken to cover the bowel incision with peritoneum at the mesenteric attachment.

Lateral Anastomosis.—In this operation there is no restoration of the continuity originally present, but a purely artificial opening is created between the two segments of intestine. Such an operation may be termed an internal enterostomy, which agrees with an external colostomy to this extent: that in each case a fistulous communication is set up. In this connection we need only describe the operations of entero-enteric anastomosis and ileocolostomy, for the gastroenteroanastomoses are considered elsewhere.

This anastomosis may be effected in several ways—preferably by suture, clamps, elastic ligature, or Murphy's button may be desirable in special cases.

Suture.—The loop of intestine is emptied and prevented from refilling by finger pressure, clamps, or gauze loops. Excision having been performed, the two cut ends are closed by the insertion of inverting Lembert sutures, the slack of the mesentery being included in the inversion. A double *cul-de-sac* thus results, the two parts of which are to be joined in the resulting lateral anastomosis. The two ends are apposed for a space of four inches or more, and a single line of Lembert sutures applied at their junction. The segments being now in their permanent position, they are incised close to the suture line with scissors. As a rule, the length of the incisions should be three inches.

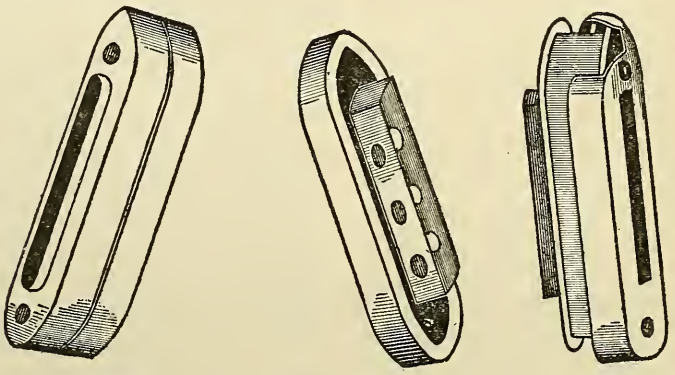
A continuous suture of chromicized gut is carried along both sides of the new opening, thus constituting the inside suture plane. The outside plane is completed by a second durable Lembert suture. Of mechanical aids, Murphy's oblong button is the best for general use, the technique being akin to that of the round button for end-to-end anastomosis.

> When making an intestinal resection, a lateral anastomosis with a Murphy button may be done with such rapidity that an immediate resection may safely be accomplished. The writer uses the Hartley method in making the lateral anastomosis, dropping half of a Murphy button into each end of the gut which is left after resection, and, after closing the ends of the gut by the Lilienthal method, pushes the halves of the button together. Lilienthal simply ties off the gut with twine instead of turning in or sewing up the end. The writer has now used it six times with six suc-

cesses. In 3 cases of strangulated hernia, he resected, made a lateral anastomosis with the Murphy button by the Hartley method, tied off the ends of the gut with fine linen or silk by the Lilienthal method, cut off the ends of the silk short, and dropped the gut back, closing the abdomen without a drain. In another case of strangulated hernia he did the same, except that, on account of the evident infection, he inserted a rubber drain down to the closed peritoneum. Wallace (Amer. Jour. of Surg., Jan., 1911).

cially multiple ones), and malignant disease.

Operative exclusion of the colon is indicated as a last resort, but in a personal case it gave excellent results, freeing the patient, a woman of 28, from intestinal disturbances of several years' standing, probably due to sagging of the colon and chronic colitis. The fistula in the cecum still persists, but causes no annoyance, and the patient has gained 20 pounds in the two years since. Hirschel (Beiträge z. klin. Chir., Dec., 1909).



Closed. Open.

Oblong Murphy button.

Enteroexclusion.—The temporary operation is not a procedure comparative to enterectomy. It is without some of the dangers of the radical operation, and may be performed rapidly. The operation consists in division of the intestine and lateral enteroanastomosis, or, in the case of the colon, enteroimplantation. A diseased portion of the intestine which would otherwise demand extirpation is then excluded from the intestine. If the distal end is closed the operation is known as partial or unilateral exclusion; but, if it is also made the subject of an anastomosis, the intervention is known as double or complete occlusion. The chief indications are tuberculosis, fistulæ (espe-

Unilateral Exclusion.—No attempt is made to close the excluded loop at its lower extremity, which is just above the anastomosis, as there is no danger of stagnation of feces in this locality. Technically the operation is well adapted for the use of Murphy buttons. No details need be given, as these are identical with the details of anastomoses after excisions. Its chief use is in emergency cases.

Bilateral Exclusion.—Both ends of the excluded loop are closed, and either two anastomoses are made or one end only is anastomosed while the other is left in the external wound. When the operation has been done for actual intestinal fistulæ, both ends of the loop may be closed, as

the loop will then be drained sufficiently through the fistulous openings. If exclusion is done for carcinoma it is better to leave one end of the loop in the external wound, for, when the operation has been done for any incurable condition, exclusion must be followed sooner or later by excision.

Enterostomy, Jejunostomy, Ileostomy.—The establishment of an artificial opening in the small intestine is not necessarily for the purpose of establishing an anus *contra naturam,* but may be done simply for relief of distention or, like gastrostomy, for the introduction of nutriment. The only condition justifying this form of intervention is an absolutely irremediable stricture of the pylorus with resulting starvation.

The operation may be done like a gastrostomy, using a tube or catheter. It is preferable, however, to sacrifice the integrity of the intestine by division and anastomosis, leaving a cut end in the external wound. The point selected is in the jejunum, about eight inches below the duodenojejunal angle. The intestine is divided at this point and the central end implanted six or eight inches farther along the gut. The peripheral end is not treated like the stomach cone in gastrostomy, *i.e.,* it is passed out of the external incision, beneath the skin, and out at a special opening (see Gastrostomy). The original wound is closed plane by plane while the fistular wound is sutured to the divided intestine.

> The writer, in an investigation of all gastrojejunostomies done by him in St. Mary's Hospital to ascertain whether jejunal ulcer had followed, found that out of 1141 gastrojejunostomies 715 were performed for duodenal and gastric ulcer, 167 for carcinomatous obstruction of the pylorus, and 259 in connection with partial gastrectomy, most of which were for cancer. Not a single case of jejunal ulcer had developed, nor did any case appear at the clinic in cases operated by other surgeons. W. J. Mayo (Surg., Gynec. and Obstet., March, 1910).
>
> Case operated on for ulcer of the stomach in which a posterior no-loop gastroenterostomy has been performed. The operation, while it relieved the original symptoms, caused frequent vomiting of biliary and pancreatic fluids, due to some spur or kink left after the anastomosis. The operation performed for the relief of this regurgitant vomiting consisted in anastomosing the ascending or terminal portion of the duodenum—just as it turns upward—to the jejunum. It is not necessarily tedious or difficult and has the advantage of producing drainage of the duodenum directly into the jejunum —a safety valve, so to speak, in the operation of the gastroenterostomy—which can be done either at the time of the gastroenterostomy operation or later if needed. Since his operation in this case, the writer has twice operated on the cadaver, and had no difficulty in pulling a loop of duodenum through the covering perit neum and making the anastomosis. The operation will not have to be done very often, but may at times be of marked value. P. S. Moncure (Jour. Amer. Med. Assoc., March 18, 1911).

Ileostomy is sometimes performed for establishing an artificial anus, necessarily in cases where ileocolostomy or simple colostomy is insufficient for drainage. The lowest possible part of the ileum is selected, the incision being made one and one-half inches above Poupart's ligament. In this operation it is not necessary to divide the intestine, and the technique does not differ from that of ordinary colostomy.

Report of 68 cases in which jejunostomy has been performed during the last ten years. The technique was Eiselberg's adaptation to the jejunum of Witzel's obliquely imbedded tube. It is a simple operation, while it insures complete continence for fluids, and the fistula closes spontaneously when its purpose has been accomplished and the drain holding it open is removed. One of its great advantages is that the patient can be well nourished until normal conditions can be restored. This is particularly important in case of ulcer. Lempp (Archiv für klin. Chir., Bd. lxxvi, Nu. 1-2, 1905).

Report of 25 operations in which jejunostomy was done by Garré at Königsberg. The operations were for cancer in 20 cases, and for ulcer or its complications in the others. One patient succumbed to hemorrhage from a hemorrhagic ulcer, another to peritonitic complications of a very large cancer, another to marasmus from carcinomatous peritonitis with ascites, and another with cancer to pulmonary embolism—a total mortality of 4 out of 25 cases. Loyal (Beiträge z. klin. Chir., von Bruns, Bd. li, Nu. 3, 1907).

Jejunostomy does not merit the discredit into which it has fallen, in the view of many surgeons. The results are good when a simple technique is employed. Preference is given to two methods of operation: the one proposed by Drucbert, in which a canal is made leading out from the intestine between the serous and the muscular coats of the intestine; the other proposed by Eiselberg and Witzel, in which the canal is made along the wall of the intestine by plicating it over a catheter as in the similar method of performing a gastrostomy. The chief object of any method is to obtain an opening in the bowel which will be continent. It should be one that can be easily and rapidly made and one that may be only temporary. More complicated operations do not accomplish more than these simple ones, and are not tolerated so well by the enfeebled patients. Delore and Thevenot (Archiv gén. d. chir., vol. ii, p. 237, 1908).

SURGERY OF THE APPENDIX.—The appendix, while nominally a portion of the colon, is subject to peculiar affections which, in themselves often trivial, are prone to give rise to the most serious surgical complications. The mere removal of the appendix makes up a small portion of the actual surgery of this organ, which includes the surgical management of appendix-abscesses, appendix-peritonitis, and other complications. Hence the description of appendectomy as a typical operation representing the surgery of the organ is a small part of the subject, and requires elaboration only because of the different complications surrounding the work.

The typical operation in a case of early infection, or in fibroid degeneration of the appendix, consists in bringing the appendix to the outside of the abdomen, ligating it like an artery with catgut at two points, one-fourth inch apart. We sever the appendix between these two points of ligation and carry a drop of 95 per cent. carbolic acid into the lumen of each stump. The scissors or knife with which the severing is done is not used again at the operation, because the instrument is now infected, and is to be put aside in a safe place. The carbolic acid has sterilized the tissues with which it has come in contact instantly, and in order to stop any further and undesirable action we neutralize the carbolic acid with a few drops of alcohol applied with a pledget of cotton.

The next step is ligation of the mesappendix with catgut at as many points as desirable in any particular case. In some cases the mesappendix allows a safe ligation with a single

ligature. In other cases where it has a particularly broad attachment, four or five ligatures may be required. It is quite as important in ligating mesappendix as in ligating broad ligament after an operation for ovariotomy, not to include too much tissue in any one ligature, and not to cut the stumps too short above the ligature, for the reason that vomiting and other movements subsequent to the operation are particularly apt to force off these ligatures and give rise to secondary hemorrhage or opening of the lumen of the appendix. The last step after cutting away the mesappendix consists in scarifying the peritoneum of the cecum near the stump of the appendix that is left, with the point of a needle, in order to insure an abundance of lymph exudation which will wall in the stump.

The author has employed practically all of the fanciful methods of treatment of the stump which have been described by authors, and has dropped all but this simple method, which saves time. At one hospital where four thousand appendectomies performed by this method have been tabulated, there were only two cases of trouble due to the form of procedure, and both of these were due to the slipping of a ligature, both ligatures having been tied by the same member of the house staff, who may not have learned to tie square knots, or who may have cut stumps too short. Where old adhesions make it difficult to bring the appendix out upon the abdominal wall, this simple method of treatment of the stump does away with many difficulties.

In cases of acute infection with abscess, with dense new or old adhesions, it is extremely unwise to attempt to bring the cecum to the surface in order to carry out peculiar methods of treatment of the stump of the appendix, and in such cases it will suffice if we snap a pair of forceps upon the appendix close to the cecum, and remove the appendix with the finger without further detail, unless one wishes to leave another pair of forceps on the mesappendix. The forceps left in place for twenty-four hours serve to protect also the small drain placed alongside. At the end of twenty-four hours the forceps may be removed, and no more attention given to the stump of the appendix. In these far-advanced cases the arteries of the mesappendix have commonly been occluded by proliferating endarteritis and the veins are filled with thrombi, so that the hemorrhage amounts to nothing more than a moderate degree of oozing cared for by the capillary drain. Such simple treatment does away with a great part of the dangerously severe part of operative work which in the third era of surgery has often been thought necessary. Treatment of abscesses and peritonitis of appendix origin is discussed under the general head elsewhere in the article.

See also APPENDICOSTOMY and the article on APPENDICITIS in the second volume of this work.

Series of 110 operations showing the advantage of simplicity in operating, with mortality. Nearly one-half of the patients were under 15 years of age. Sixty-four were acute cases, the patients being operated upon either in the interval or at a late non-purulent stage. In 44 acute cases, operation was done on the first, second, or third day. Two patients were operated upon the fourth day, 1 on the fifth, 1 on the sixth, 4 in the seventh, 5 on the eighth, 2 on the tenth, 1 on the eleventh, 3 on

the twelfth, and 1 on the twenty-third day. This tends to show that the risk of operation on any particular day is not unduly great. The writer emphasizes the advantage of a small incision, the quick drainage of the appendicular site if pus is there, the removal of the appendix only if it is easily reached, the absolute neglect of the remainder of the peritoneal cavity except as it may be favorably influenced by the drainage. Dowd (Annals of Surg., Oct., 1909).

The writer has lost no patient upon whom he operated within thirty-six hours of the attack. During the past five years he has had nine deaths following operations performed between the second and eighth days of the attack. Only one of these deaths occurred in his hospital practice, and others were all after operation performed at the homes of the patients.

When a patient suffering with appendicitis of more than forty-eight hours' duration cannot safely be transported to the hospital, he should be put on the Ochsner treatment and operation postponed until the acute inflammation has subsided. When the abdomen has finally become flat, pain and tenderness have disappeared, and the pulse and temperature have become normal, the appendix may be safely removed. Collins (Ill. Med. Jour., Oct., 1909).

Chronic appendicitis, so-called, is not always relieved by appendicectomy. A Lane kink near the ileocecal valve may be the real cause of obstruction and simulate the above condition. The main symptoms as described by Stierlin are as follows: There are attacks of colic, mainly located in the region of the cecum and ascending colon, unaccompanied by any rise in temperature, and often associated with continued painful sensations in this region; the pain may also involve the region of the stomach. It may last for a longer or shorter time. Chronic obstinate constipation is present, alternating with short periods of diarrhea; these latter usually occur at the end of an attack of colic. A tumor of a balloon-like character is felt in the region of the cecum, which, upon palpation, gives forth gurgling sounds, and which may or may not be painful; it is often distinctly movable. Hofmeister (Beitr. z. klin. Chir., Bd. lxxi, Hft. 2, 1911).

Colostomy.—Now and then it becomes necessary to perform colostomy for patients suffering from chronic obstruction induced by a growth, stricture, angulation, adhesion, volvulus, invagination, foreign body, diverticulum, or enteroptosis, after other measures have been tried and failed. Again, an artificial anus is sometimes made to relieve patients suffering from membranous catarrh, the various types of ulcerative colitis and multiple polypi, but this procedure is not so popular for this purpose as it was before the advent of appendicostomy and cecostomy.

An artificial anus should never be made except as a *dernier ressort* because of its unnatural location, the odors which emanate from it, the necessity of wearing a bandage, and, further, because a serious operation is required when the time for its closure arrives.

An artificial anus may be temporary when made as a preliminary step to excision and resection or until such time as the condition, for the relief of which it was made, has been cured; or permanent, when the opening is to remain through life.

It is not necessary to spend as much time in the formation of a temporary anus as it is in the making of a permanent anus, because the former is to be of short duration and the patient can bear the annoyance for a short time. In permanent colostomy it is of the utmost importance to provide for the patient's comfort by making the opening in such a way

that he may not have painful evacuations, complete fecal incontinence or procidentia.

Formerly there was considerable discussion as to which was the better procedure, inguinal or lumbar colostomy; but lately the latter has fallen completely into disuse because the operation is more difficult, a suitable spur cannot be made, and the anus is situated where the patient cannot easily attend to it, while the former operation is devoid of all of these disadvantages.

Except where there are special reasons for doing otherwise, the colonic aperture should be made of fair size and as low down in the bowel as possible, because here the feces are more solid and give less trouble than when the anus is established at or near the cecum. An anal opening should never be made in the small bowel because when this is done there is a constant discharge of fluid through it, which annoys the patient and keeps the skin continually excoriated.

The majority of surgeons concentrate their efforts toward the formation of a proper spur and the production of the double-barrel-gun effect, to prevent any of the feces from reaching the rectum, but do comparatively little toward providing an anus over which the patient can exert a fair degree of control.

The Murphy button is a suitable and proper instrument for the establishment of an anastomosis in the large intestine. The danger that the anastomosis with the button will not be efficient when proper technique is used in connection with a good button is no greater than when anastomosis is made by means of sutures. The chief danger from the button lies in the arrest of the button by means of dried fecal matter or a foreign body, as a cherry or plum stone. In the after-treatment it should be seen that the bowels are emptied at proper intervals. At the first indication of obstruction of the bowels the anastomosis should be examined. The Murphy button in the large intestine affords the easy technique and the brevity of the operation it does elsewhere. Mühsam (Deut. Zeit. f. Chir., Bd. 105, Hft. 3-4, 1910).

Report of 19 cases of primary resection of the large intestine at von Eiselberg's clinic at Vienna. Three of the patients did not survive the operation; one of this group had had a febrile sore throat a short time before, and the fatal peritonitis was due exclusively to streptococci. The operation should have been postponed to allow time for the streptococcus infection to die out. In another similar case, although the patient recovered, yet streptococcus peritonitis followed the angina and streptococci could be cultivated from the blood. In the third case the patient was doing well up to the fifth day after extensive resection of stomach and intestine, but then a suture on the ascending colon gave way. In all the other cases the wound healed by primary intention. Haberer (Archiv f. klin. Chir., Bd. xciv, Nu. 4, 1911).

Gant's Colostomy.—The sigmoid is reached and isolated through a two-inch incision which crosses a line extending from the umbilicus to the anterior superior spine of the ilium, at the inner border of the oblique muscles; working outward, the transversalis is separated from the internal oblique muscle, with the index and middle fingers, for about one and one-half inches. The fingers are then forced upward through the oblique muscles and then over the external oblique and inward to the incision, separating the subcutaneous fat from the muscle. A loop of the sigmoid is now hooked up and then made to traverse the

route taken by the fingers, which makes it pass outward between the internal oblique and the transversalis muscles, and then through the internal and external obliques and finally over the latter back to the incision. Again, when it is sutured after being made taut to avoid the possibility of subsequent procidentia, the angles of the wound are approximated by two chromicized catgut sutures, which pass through the skin and fascia on one side of the incision and then beneath the longitudinal band of the sigmoid and out through the same structures on the other side, where they are tied. After the gut has been attached to the skin by a few plain catgut sutures it is surrounded by a bird's nest dressing to prevent its being pressed upon, covered with rubber tissue lubricated with sterile vaselin to prevent sticking of the gauze to the bowel, and then the outer dressing and binder are applied.

The intestine is not opened until after the third day, except when there is a marked distention; under such circumstances it is punctured at any time after six hours and amputated later. The projecting piece of gut is quickly and painlessly removed by injecting a small quantity of a one-eighth per cent. eucain solution into its mesentery. Cutting of the bowel proper causes no pain and does not require anesthetizing.

By a few cuts of the scissors, the intestine is amputated about one-quarter of an inch from the skin, bleeding points are ligated *en masse*, and hemorrhage from oozing surfaces is controlled by hot-water compresses or the cautery. The raw edges left are encouraged to heal rapidly by the occasional application of 6 per cent. silver nitrate. When the obstruction is located above the sigmoid, the steps in the operation must necessarily be modified to meet the indications, but the changes in the technique will suggest themselves to the surgeon in individual cases.

Patients have but little control over an artificial anus for the first few days, no matter what operation is performed, because the soreness of the wound and the irritability of the intestine excite frequent and strong peristalsis and the involuntary discharge of the feces.

This procedure has the advantage over other colostomies in that but one incision is made and, further, because it gives the patient a more perfect control over the movements than do other colostomies.

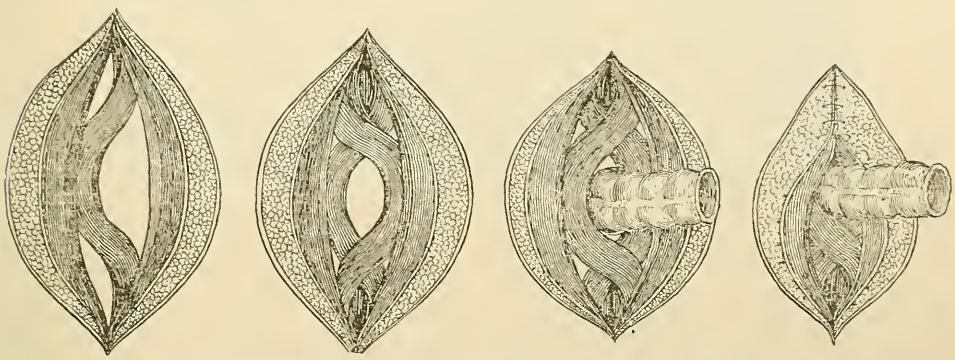
According to Gant, patients operated upon in this way except during the first few days rarely complain of the involuntary escape of gas and ordinarily do not have an evacuation until they have taken a mild laxative or stimulated peristalsis by a small enema.

It requires very little time to perform colostomy for a patient and the operation is practically devoid of danger, but the reverse obtains in the operation for its closure, as usually done by intestinal anastomosis.

To avoid the dangers which accompany joining of the two ends of gut, Gant has devised a special plan for closing artificial ani. Some years ago he invented a clamp, which has proved useful in the closing of colostomy openings. Its weight is imperceptible to the patient, and when in place the shank, which is bent at an angle to the clamp, lies flat upon the

abdomen. The jaws are fenestrated, one-half inch broad and one and one-fourth inches in length. It is applied as follows: The clamp is placed in the applicator forceps, which are so adjusted that the jaws of the clamp remain open to the fullest extent. The parts having been cleansed, the partition between the upper and lower colostomy openings is stripped to dislodge any coil of the intestine which might otherwise be injured.

The writer describes the following method calculated to insure sphincteric control after colostomy: The rectus is split vertically and the sigmoid is drawn out and divided at a convenient point. The lower segment is closed and replaced in the abdomen. The upper segment is made less bulky by removing the appendices epiploicæ and freeing it of mesenteric fat, but without in any way interfering with its blood-supply. The artificial sphincter is then made in the following manner: A loop of muscle-fibers is separated



Operation for sphincter control after colostomy. (*Ryall.*)
(Clinical Journal.)

The clamp is then applied, one blade in each opening, and pushed down sufficiently to include the entire spur, when it is released from the instrument. It is allowed to remain *in situ* until the spur is divided and it comes away unaided, which is usually from six to nine days later. The clamp causes slight soreness, but no acute pain. To avoid complications, the patient had best remain quietly in bed until it sloughs out. When the partition has been successfully destroyed the skin and edges of the opening are freshened under local anesthesia and closed with catgut or silk, and, in case there is considerable tension, the wound is supported by well-adjusted adhesive straps.

from the posterior aspect of the rectus on either side of the wound. Each loop is then drawn over to the opposite side of the wound, so that one loop overlaps the other. The overlapping loops thus form a ring and through this the bowel segment is drawn. Sutures are then inserted to keep the muscle-fibers together above and below where the bowel comes through. Anchoring stitches are inserted through the skin and muscle inside to keep the bowel in position. The wound is then closed above and below the bowel, and the cut edges of the latter are sutured to the skin. A double sphincter is thus formed consisting of longitudinal and circular fibers. The longitudinal fibers are those of the anterior portion of the rectus, and the circular fibers are formed by the loops from the posterior part of the rectus. This operation can be modified by making double loops on each side and making them overlap one

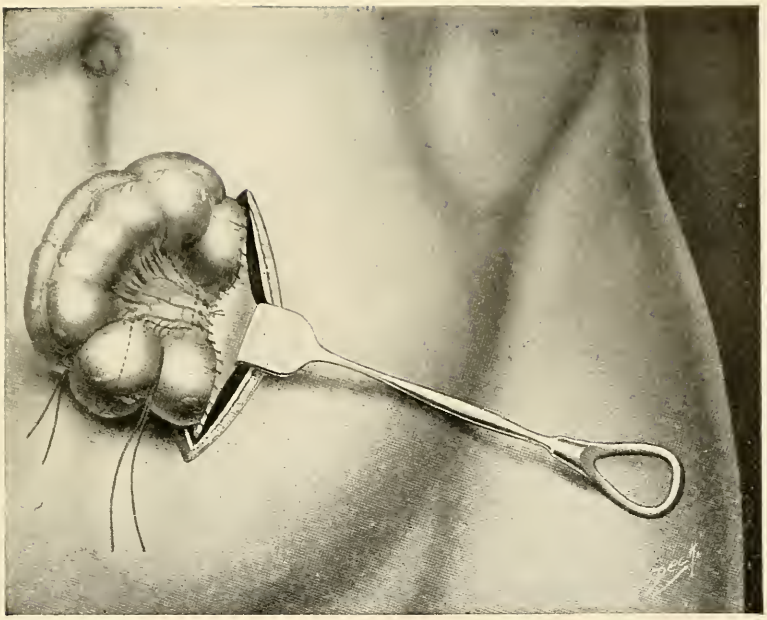
another alternately. A similar operation can be, and has been, carried through the external oblique, and likewise can be done wherever the bowel is brought through muscle. A somewhat similar operation can be performed for gastrostomy and appendicostomy. C. Ryall (Clinical Journal, Nov. 11, 1908).

Lilienthal's Colostomy.—The formation of an artificial anus for the permanent relief of obstruction of the lower bowel is regarded by most surgeons as a loathsome makeshift for the prolongation of life. The mental picture of such an opening suggests the constant uncontrollable discharge of feces and flatus, the painful and annoying dermatitis in the neighborhood of the exposed mucosa, and the necessity for constant change of dressings—in short, a condition of actual and permanent disability for the ordinary duties and pleasures of life.

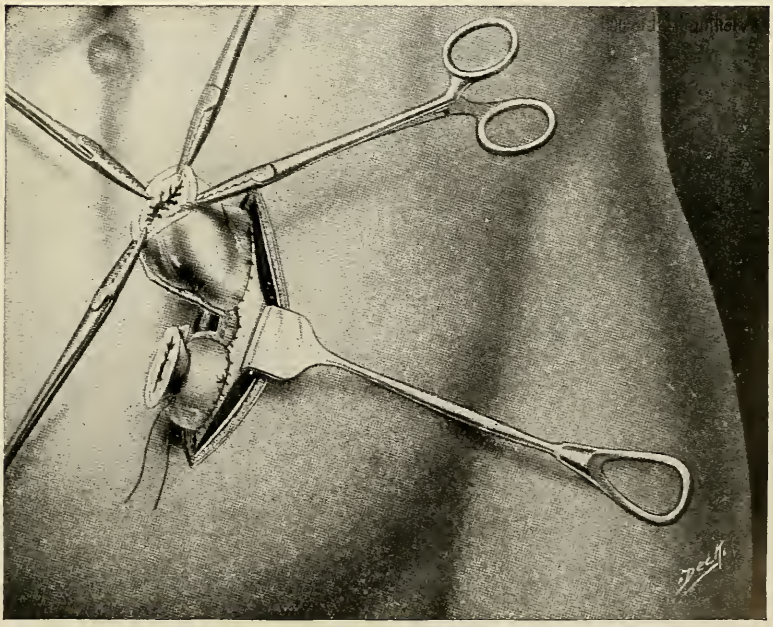
For at least eight years Lilienthal has been performing an operation which obviates nearly all the discomfort and filthiness of colostomy. The patients have absolute control of the bowels and can even hold a considerable quantity of fluid injected into the colon. The bowels move once or twice a day, the patient knows when the movements are about to occur, and—not by any means the least advantage—he is not annoyed by the necessity for wearing an appliance for obturation. The operation has been tested many times, and the patients have been for the most part carefully followed up. A description of the steps of the operation follows:—

An incision about 3½ inches long, more or less, is made over the outer third of the left rectus muscle and parallel with its fibers. The upper end of this incision is just about on a line between the umbilicus and the left anterior superior iliac spine, but the exact length and location of the wound depends somewhat on the amount of subcutaneous fat present. Through this incision the fingers explore the abdominal organs and the type and limitations of the stricture or tumor are learned. The sigmoid flexure, be it well developed or not, is drawn out. As is well known, this part of the intestine varies greatly in length, but all is taken out which can be withdrawn without tension. The two legs of the loop are separated as widely as possible, the upper leg being sutured to the peritoneum and posterior rectus sheath in the upper angle of the wound, and the lower is sutured in a similar manner to the inferior angle. Silk or linen thread is the suture material, and the stitching is done by the continuous method, every third stitch being tied so as to avoid purse-stringing. The mesosigmoid is now sutured through and through to the peritoneum on each side (Fig. 1 in the annexed plates).

At the lower leg of the loop the gut is doubly ligated very tightly with heavy silk or cotton twine. Section is carefully made between the ligatures, taking care to avoid soiling from the small amount of imprisoned intestinal contents. Pure carbolic acid on a gauze sponge is used to sterilize the mucosa. Chain ligatures of catgut or silk are now passed through the mesosigmoid so as to prevent hemorrhage, and this membrane is then cut across. We now have a short piece of sigmoid, the distal leg of the loop in the lower angle of the wound, and a long piece sutured in the upper angle of the wound. The remainder of the mesosigmoid is cut away from the long piece of intestine, freeing it completely. The entire wound is now protected by gauze pack-



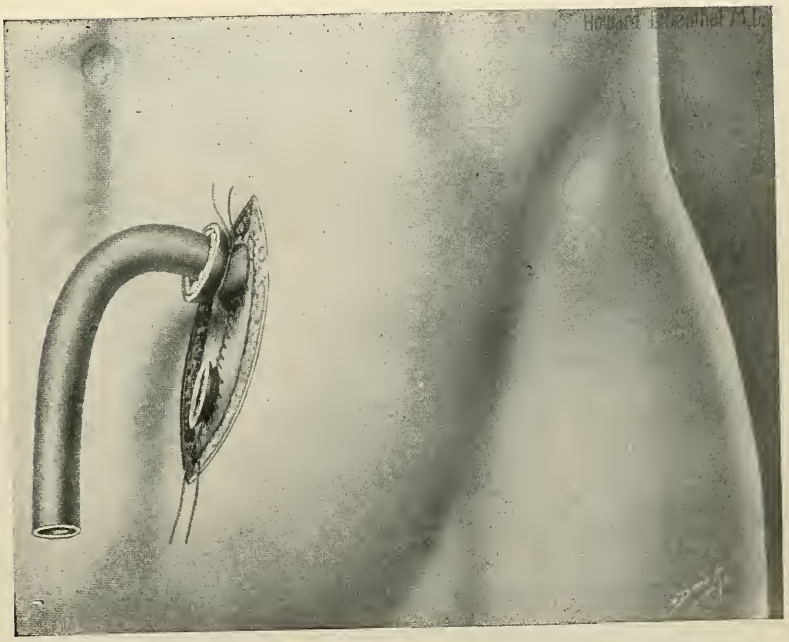
The Dotted Line Shows Line of Section. The Blunt Retractor Holds Outer Third of Rectus Muscle Together with Skin and Aponeurosis. (*Howard Lilienthal.*)
Annals of Surgery.



Redundant Bowel and Mesocolon Cut Away. Twisting of the Intestine Begun. (*Howard Lilienthal.*)
Annals of Surgery.

Twist Complete and Maintained in Position by Anchor Sutures Holding Sigmoid to Aponeurosis. (*Howard Lilienthal.*)

Annals of Surgery.



Operation Complete. Aponeurosis Further Stitched to Intestine and Wound Closed with the Exception of the Skin. (*Howard Lilienthal.*)

Annals of Surgery.

ings, the peritoneum by our previous procedures being entirely closed off by suture. We should have about 3 or 4 inches of free sigmoid at the upper angle of the wound. If there is more it should be ablated. Four equidistant clamps are now placed at the edge of this upper piece of intestine; the gloved finger is inserted into the lumen of the gut to the place where it is held to the peritoneum by suture; an assistant rotates the clamps so as to twist the gut around its longitudinal axis, after the manner described by Gersuny, from 180 to 360 degrees according to the texture and thickness of the walls of the sigmoid with which we are working. By withdrawing and reinserting the finger from time to time the degree of constriction which this maneuver produces may be accurately gauged. When this seems to be sufficient for the purpose—a matter of individual judgment—a few interrupted silk or linen sutures passed through the visceral peritoneum and submucosa to the aponeurosis of the external oblique hold the rotated gut in position. It is now necessary to make sure by re-examination that a sufficient twist has been accomplished. If this seems satisfactory more sutures should be put in to hold the gut firmly to the aponeurosis.

In examining with the finger now we find a double sphincter, the first one at the twist; the second, more an angulation than a sphincter, at the point of peritoneal fixation. A few chromic gut sutures close the portion of the remaining wound in the aponeurosis. The sphincteric action is maintained by the fibers of the rectus muscle as well as by the twist in the intestine. A large-sized, rather stiff-walled rubber rectal tube, not a woven one, is now inserted about six inches into the intestine and is tied in place, a single light suture passing through its walls guarding against its accidental extrusion. The remainder of the wound is left open and packed with gauze while the tube is led off into a receptacle at the side of the bed. These wounds always become more or less infected, but I have encountered a true phlegmon only once and then a single incision sufficed for its drainage.

About a week after the operation the tube may be withdrawn and the redundant sigmoid burned off with the actual cautery. Anesthesia is not necessary. Even then it will be found that repeated cauterizations will be required during the course of the healing in order to bring the intestinal mucosa to the skin level. Daily irrigations through the tube should be practised so as to keep the patient's bowels open. The string around the lower piece of intestine should be removed in three or four days; otherwise, there might be danger of complete and permanent closure, and it is necessary to maintain patency here for the sake of drainage.

The control of the bowels is learned gradually by the patient, and he is assisted by a constipating diet and, for the first few weeks, small doses of deodorized tincture of opium and of subgallate of bismuth, 20 grains three to five times a day. It takes about a month for the final result to be attained, but the functional result in all uncomplicated cases will be found perfect.

Appendicostomy and Cecostomy.—These operations are useful in the treatment of disease located in the colon, but, when the disturbance lies within the small bowel or involves it

and the large intestine, Gant's cecostomy, which provides a means by which the treatment can be directly applied to both, should be substituted. It is frequently impossible to determine whether the disease is limited to the colon or not, and because of this and the fact that this operation is no more difficult or dangerous than appendicostomy and ordinary cecostomy, and is equally effective both when the lesions are located in the small intestine, the large bowel or both, Gant believes his to be the most desirable procedure and that eventually it will be employed almost, if not quite, to the exclusion of appendicostomy and cecostomy in the direct treatment of intestinal affections.

Appendicostomy.—Some surgeons do not open the appendix during the operation because they fear infection. This practice, Gant believes, is bad except when it is obvious that the appendix is not obstructed, because he has encountered three failures following it; in one the appendix was too short, in another it was strictured, and in still another it was blocked by an encysted grapeseed.

He immediately amputates the appendix and introduces the probe-pointed appendiceal irrigator, then nothing can interfere with postoperative irrigation, but when the appendix is diseased it is removed and cecostomy is performed. It is important that the irrigations be started at once when patients suffering from ulcerative colitis are despondent, greatly debilitated, have many movements, lose considerable blood, and suffer from insomnia and autointoxication.

To meet these conditions Gant has devised a technique for appendicostomy which provides for irrigation both during and following the operation, since the adoption of which his patients have gained very much more rapidly than formerly, when the appendix was not opened for several days, during which time nothing was done to relieve them. Now and then a stitch abscess has occurred, but other complications have not arisen during or following the operation. Briefly described, the following are the steps: 1. The appendix is approached through a gridiron incision and located by tracing the anterior longitudinal band downward, when it and the cecum are freed and brought outside. 2. The cecum is drawn first to one side and then the other by an assistant, while the parietal peritoneum is removed at the sides of the incision to insure union between it and the transversalis fascia, or the peritoneum is left intact when the gut is to be brought into contact with it. 3. The appendix is freed and straightened by ligating and dividing adhesions and the mesentery at about one-fourth inch from it. 4. After the cecum has been scarified, two seromuscular suspensory sutures are introduced on either side and near the base of the appendix, each taking three bites in the gut. 5. By means of a strong, long-handled needle, the anchoring stitches are in turn carried through the entire thickness of the abdomen and clamped with forceps, but when the intestine is joined directly to the peritoneum the bowel is anchored by chromicized gut sutures, including the parietal peritoneum and transversalis fascia. 6. Having surrounded the appendix with gauze, a traction suture is introduced to steady it while it is being ampu-

tated, cauterized, and probed. 7. A Gant appendiceal irrigator closed with a stopper is introduced and the appendix ligated above it. 8. The appendix is placed in the lower angle of the wound, pointing upward to prevent leakage later, and anchored by two seromuscular chromicized-gut sutures, which include the transversalis fascia. 9. The abdominal layers are then separately approximated by interrupted or continuous stitches, after which the cecal suspensory sutures are tied across rubber tubes. 10. The appendiceal irrigator is prevented from slipping out by the adjustment of adhesive straps or by means of attached pieces of tape which encircle the body. 11. In urgent cases from one to three pints of a warm **saline solution** are immediately injected into the colon, when the stopper is introduced to prevent leakage. 12. The wound is sealed by means of cotton and collodion, and is protected further by split gauze pads which overlap each other when placed about the appendix. 13. The outer end of the irrigator is surrounded by twisted gauze strips to prevent pressure upon it when the outer dressings composed of gauze pads or cotton and a many-tailed binder are adjusted.

Appendicocecostomy.—On six different occasions Gant has been compelled to abandon appendicostomy for cecostomy because the appendix was too short, strictured, or blocked by a grapeseed which rendered it unfit for irrigating purposes or had sloughed off following appendicostomy. In each instance, after the appendix had been amputated or inverted, a catheter was introduced through the appendiceal stump or opening and fastened by a purse-string suture introduced at or near its base. The cecum was suspended and the rest of the operation performed as in appendicostomy.

Two patients suffered from diarrhea induced by ulcerative lesions in the colon. In these cases the catheter was introduced a short way into the cecum, providing for colonic irrigation.

The others were afflicted with enterocolitis, and it was thought advisable to irrigate both the large and small intestines. This was accomplished by guiding a catheter across the cecum through the ileocecal valve into the small bowel. This procedure is termed "appendicocecostomy."

The principal objections to this operation are (1) that a change of catheters is impossible because the appendiceal and ileocecal openings are nearly on the same level, and (2) because the appendiceal aperture is so small that two catheters of sufficient size cannot be introduced to provide for large and small bowel irrigation.

Cecostomy.—Experience has demonstrated to Gant's satisfaction that cecostomy is preferable to appendicostomy in the direct treating of intestinal disease. A comparative study of the advantages of cecostomy and the disadvantages of appendicostomy, as enumerated below, will show why the former should take preference over the latter.

The advantages of the cecostomy operation, and more especially the writer's cecostomy, which provides a means of irrigating both the large and small intestine, are: 1. Owing to the fact that the cecum lies against the inner abdominal parietes, it can be easily anchored without angulating

or twisting the bowel. 2. Since the opening is opposite the ileocecal valve, a catheter can be introduced into the small bowel for irrigating purposes or the siphoning of its contents for examination. 3. The cecal opening can invariably be made of a suitable size. 4. The circular, valve-like projection formed around the catheter by the infolding purse-string sutures prevents leakage. 5. The catheter can be changed without difficulty. 6. Closure of the opening follows withdrawal of the catheter and a few applications of the copper stick or cautery. 7. Owing to the natural position of the cecum, there is less tension and pain following its anchorage to the abdomen than occurs after appendicostomy. 8. This cecostomy may be employed in the treatment of lesions located anywhere in the intestinal canal, while appendicostomy is limited to those in the colon.

The disadvantages of appendicostomy are the following: 1. The appendix is more difficult to bring up for anchorage than the cecum because of its deeper and more uncertain position, and because it is frequently bound down by adhesions or a short mesentery. 2. Anchoring of the appendix causes angulation or twisting of the cecum, which, in turn, may induce constipation, discomfort, or pain. 3. When the cecum about the appendiceal base is caught in the wound, it induces nausea and vomiting until detached (writer's case). 4. When the appendix is small, short, strictured, bound down by adhesions, blocked, or is otherwise diseased, it is useless for irrigating purposes. 5. Irrigation is frequently difficult and unsatisfactory because of the small appendiceal opening. 6. Pain following appendicostomy is much greater than after cecostomy owing to the pulling upon the appendix by the loaded cecum, the periappendiceal adhesions, or the squeezing of the attached mesentery when the wound is closed tightly about it. 7. Frequent dilatation or the insertion of a catheter is often necessary to keep the opening sufficiently large. 8. Death has followed injection of the irrigating fluid into the abdomen beside the appendix where an interne mistook an opening in the wound for that of the appendix. 9. After a cure it is more difficult to close the appendiceal than the cecal outlet, and frequently appendectomy is imperative. 10. Appendicostomy frequently fails because the appendix slips back into the abdomen or retracts sufficiently to make irrigation almost or quite impossible. 11. The appendix has been known to slough off on several occasions owing to tension, its constriction by the sutures or destruction of its blood-supply making subsequent cecostomy necessary. 12. Appendicostomy is not effective when the disease is located in the small intestine. 13. Appendicitis requiring appendectomy following closure of the appendiceal outlet has occurred. 14. Owing to the irritation caused by the catheter or treatment the mucosa may become so inflamed and swollen, ulcerated or strictured, that irrigation must be abandoned. 15. Finally, according to Reed, the catheter causes the wall of the appendix frequently to perish in a few days.

Cecostomy with an Arrangement for Irrigating both the Small Intestine and Colon.—Gant has described what he believes to be an original way of irrigating both the small and large bowel

through the same opening in the cecum—an operation which, for want of a better name, he has designated "cecostomy with an arrangement for irrigating both the small intestine and colon."

He believes his cecostomy is superior because the technique is simple, the operation requires no more time than others, there is less leakage owing to the purse-string infolding being substituted for his lateral sutures, both the small and large bowel can be irrigated by the attendant or patient, a firmer support is obtained by attaching the cecum to the transversalis fascia than to the parietal peritoneum, and the opening heals spontaneously after the catheters are removed.

Briefly described, the steps in Gant's cecostomy are: 1. Through a two-inch intermuscular incision made directly over the cecum, it and the lowermost part of the ileum are withdrawn and the edges of the wound covered with gauze handkerchiefs. 2. The anterior surface of the cecum is scarified after the ascending colon and ileum have been clamped to prevent soiling of the wound when the bowel is opened. 3. Four linen seromuscular purse-string sutures are introduced into the anterior wall of the cecum opposite the ileocecal valve, and the bowel is opened inside the suture line. 4. The gut is grasped at the juncture of the large and small intestines and held in such a way that the ileocecal valve rests between the thumb and fingers of the left hand. A Gant catheter guide is then passed directly across the cecum and through the ileocecal valve into the small intestine, aided by the thumb and fingers. 5. The guide is held by an assistant while the obturator is removed and a catheter is introduced into the small bowel. It is then removed and the catheter firmly held in the small gut by an assistant until anchored to the cecum by catgut sutures to prevent its slipping out during the operation. 6. A short rubber tube three inches long is projected into the cecum for an inch or more and anchored beside the one in the small gut. 7. The infolding purse-string sutures are now tied, forming a cone-shaped valve above the catheters to prevent leakage of gas and feces. 8. After removal of the clamps, the cecum is scarified and anchored to the transversalis fascia, denuded of its peritoneum by through-and-through suspension sutures of linen, or by chromicized catgut stitches, including the fascia, when the two peritoneal surfaces are to be approximated. 9. The wound is closed by the layer method and the catheters are fastened by stitching or by encircling them with an adhesive strip to hold them together, and crossing this at a right angle with a second piece of plaster placed between the catheter to prevent their slipping out. 10. The ends of the catheters are closed with cravat clamps to prevent leakage, and the operation is completed by applying the dressings above the projecting tubes.

One catheter is left longer than the other or is identified in some way in order that the interne or nurse may know *which is in the large* and *which in the small intestine* when time for irrigation arrives. To avoid danger from infection treatment is not begun before the fifth day except when urgent.

The catheter may be readily changed by cutting the attached adhesive strips and withdrawing the one projecting into the cecum. Gant's catheter guide is then passed over the other into the small intestine, where it is retained until the old tube has been removed and a new one introduced. A second piece of catheter is then placed in the cecum and both are prevented from slipping out by adjusting fresh adhesive straps after the manner already described.

Before deciding upon the above technique Gant irrigated the small intestine by passing a glass or silver catheter through a cecal opening, past the ileocecal valve, into the small gut each time it was irrigated, but this practice was abandoned as impracticable because of the difficulty encountered in locating and passing the valve, and, further, because the patient could not irrigate himself in this way.

Gant has had no reason to suspect that peristalsis forced the catheter out of the small intestine into the cecum except in one of his first cecostomies, where the tube was cut short and projected only one inch beyond the ileocecal valve instead of several, as it should. He feels confident that the catheter remained in the small gut in his other cases because (*a*) water injected through the colonic pipe was evacuated much quicker than when it was deposited in the small bowel; (*b*) when a minute quantity of a 10 per cent. solution of methylene-blue was injected through the former, it appeared in the urine more quickly than when introduced through the catheter in the small gut, and (*c*) the catheter guide could be carried over the tube in the small intestine and the latter could be removed and replaced with a new one at will, and, further, (*d*) fluid feces could be withdrawn more quickly and frequently through the pipe in the small intestine than through the colonic catheter.

To avoid possible expulsion of the catheter from the ileum, catheters made of silk, silver, glass, and soft rubber reinforced by an inner metal tubing which cannot be forced out of the bowel owing to their non-flexibility are employed. Only that portion of the latter projecting into the small bowel was reinforced, and as a result it served the desired purpose and caused but little irritation because it was soft and flexible. This cecostomy permits the attendant or the patient to irrigate the small and large intestines at will, and the fluid may be siphoned or allowed to escape through the anus and the catheter can be changed quickly as often as is necessary.

Enterocolonic Irrigator.—An instrument successfully employed by Gant several times in the direct treatment of intestinal affections involving both the large and small intestines. It is made both of rubber and metal, and has worked exceedingly well in the few cases in which it has been used.

When it is in position, the attached inflating bag lies in the small intestine at or near the ileocecal valve, and when distended prevents the escape of the solution into the cecum, thereby enabling the attendant to accurately gauge the amount of fluid deposited in the small bowel and to retain it there as long as required. By means of this twin-tube irrigator, the small and large intestines can be quickly and scientifically flushed,

singly or together, by the physician, nurse, or patient.

The steps in cecostomy, when the irrigator is employed, are similar to those already described when separate catheters are used, except that the Gant catheter guide is unnecessary and the apparatus is retained in position by attached pieces of tape which encircle the body.

Indications for Direct Bowel Treatment.—This form of treatment has a much wider field of usefulness than the profession at present realizes. Most physicians and surgeons who have practised it at all appear to labor under the impression that it is limited to the colon and is indicated *only* in ulcerative lesions of the large bowel causing diarrhea.

Gant has called attention to the fact that this type of cecostomy is indicated in the treatment of intestinal parasites, enteritis, enterocolitis, and catarrhal, tuberculous, syphilitic, dysenteric and gonorrheal colitis; ordinary and pernicious anemia; the many manifestations dependent upon intestinal autointoxication, ptomain poisoning, diarrhea of adults and children, intestinal feeding, malnutrition, and following operations upon the mouth, throat, esophagus or stomach; in gastric stricture, ulcer, cancer and other disturbances where rest of the organ is indicated. Gant also called attention to the fact that by means of his cecostomy various intestinal diseases could be investigated, and that the procedure could be used to determine the amount and nature of the intestinal juices and discharges, the character of the feces, the action of salines and other cathartics injected directly into the small and large bowel, and the marked immediate vasomotor effect following hot and cold enteroclysis and many other interesting problems.

The writer has reported several cases successfully treated by his operation. While he has had no personal experience with it in the treatment of cholera and typhoid fever, he believes that it is indicated and in the future would be used in the treatment of these and nearly if not all other non-obstructing diseases of the small and large bowel.

Gant has also pointed out the usefulness of appendicostomy and cecostomy as a means of drainage when the cecum or other part of the colon was excluded. He has also employed appendicostomy and cecostomy a number of times when operating for mechanical constipation where colitis was a complication, and also in the palliative treatment of obstipation where the patient declined to have the cause of the obstruction removed and yet suffered from deplorable autointoxication or recurring impaction.

Gant has also performed cecostomy once for the relief of septic peritonitis, but the patient was almost moribund and the operation failed. Reed was more fortunate in the two cases in which he resorted to cecostomy. This authority has also recorded a case of "defective flora" of the colon which was improved by the injection of the needed bacteria through a cecostomy opening, has called attention to its usefulness in the treatment of intussusception, and emphasizes many other important points concerning cecostomy and appendicostomy.

Following direct treatment, the condition of the patient becomes rapidly better and manifestations

such as anemia and those induced by autointoxication rapidly disappear, and in cases of diarrhea the frequency of the stools generally diminishes and the amount of blood, pus, and mucus passed becomes markedly less.

The good results following the **irrigating treatment** are due mainly to the mechanical action of the fluid in cleansing and stimulating the ulcers and removing retained toxins, and not to its temperature or chemical contents. Solutions should always be employed at the bodily temperature or warmer because of their soothing effect upon the irritated bowel, and not cold or at a freezing point, as recommended by some authors, because when injected ice cold they excite enterospasm and cause much unnecessary suffering.

Briefly stated, the most reliable, stimulating, and soothing remedies to employ are **weak solutions of boric acid, quinine, formalin, hydrastis, krameria and soda, silver nitrate,** and those of a soothing nature are **kerosene, liquid paraffin** or **olive oil,** according to indications. The stimulating solutions are used stronger when ulceration is extensive and the oils warm when the gut is irritable.

Owing to our recent knowledge of diseases of the colon, the internists agree that the treatment of these diseases by medication is generally unsatisfactory. The great length of the intestinal tract and the many chemical changes taking place before medicaments reach the colon are the two principal reasons why cecectomy or appendicostomy should be practised. The posterior position of the appendix and the necessity for rotating the colon about half way on its axis, the possible sloughing of the appendix are the chief reasons why cecostomy should be done instead of appendicostomy. The technique is as follows: A gridiron incision is made, the cecum brought up and held by rubber-covered forceps, and a suitable point selected for the fistula.

This opening preferably should be made opposite the ileocecal valve, so that irrigation of the small intestine can be done as easily as of the large intestine; 2 or 3 purse-string sutures of linen are inserted, and a small opening made in the bowel with scissors. A No. 10 soft-rubber catheter is inserted into the bowel for a distance of about four inches; the sutures are tied, inverting the head of the colon, which produces a valve at the point, and prevents leakage. The cecum is attached to the parietal peritoneum with chromic catgut. The catheter should be fastened to the abdominal wall by one silk suture. The diseases which most frequently require cecostomy are amebic dysentery, tuberculosis, hemorrhage, ulcerations, colitis, chronic catarrhal colitis, and syphilitic colitis. W. M. Beach (Penna. Med. Jour., March, 1911; Amer. Jour. of Gastroenterology, June, 1911).

Colectomy.—Excision of the colon is performed for malignant disease, including tuberculosis and gangrene, but in practice the operation, like colostomy, is confined to cecectomy and sigmoidectomy, unless the morbid process directly involves the transverse colon, where the hepatic or splenic flexure is usually the seat of the disease.

Cecectomy.—This operation, while so named, is by no means limited to the cecum, for it is usually necessary to remove either the ascending colon or a portion of ileum or of both intestines together. Hence such intervention may be termed ileocolectomy, ascending colectomy, etc., according to the individual case.

The incision is made in the middle line, unless the diagnosis has been made so well that the operator can

incise directly over the growth. As in all similar cases, the gut is mobilized, brought out and walled off with gauze, while it is emptied and clamped or held empty by assistants' fingers or tape. The technique differs little from that of enterectomy of the small bowel. The mesentery is tied off and then divided, the large bowel excised and the operation completed by restoring the continuity of the intestine. As the cecum and appendix have been sacrificed, it is necessary to secure an anastomosis between the ileum and transverse or descending colon.

An end-to-end anastomosis is hardly practicable because of the disparity in size between the small and large bowel. Hence a lateral anastomosis or an implantation is indicated, which may be made by suture or button. The technique is that usually pursued in all intestinal anastomoses.

Lateral anastomoses are practicable when the ileum is to be united with the neighboring ascending colon.

No attempt is made to provide for a cecal pouch or ileocecal valve, but the two ends are joined after the cut end of the colon has been closed.

It is sometimes advisable to implant the ileum in the descending colon or sigmoid flexure (ileosigmoidostomy). This would be necessary if the ascending colon were sacrificed.

The general tendency is to regard total resection as indicated only when all other methods of treatment have failed. The writer reports a case in which after exposure of the intussusception which involved the ileum about a hand's breadth from the cecum it was found impossible to reduce the invagination. It was resected and the bowel ends united by circular suture. The patient recovered and was discharged one month after the operation. Three months later the patient was again examined and found well, and six months pregnant. She was delivered successfully. Leichenstern found that in 479 cases of invagination spontaneous reduction of the invagination occurred in 15 cases; also in 15.6 per cent. of the cases of invagination of the ileum, with a mortality of 42.6 per cent. We cannot, therefore, rely upon this method of treatment. The writer agrees with Rydigier in the following conclusions on the treatment of intussusception: In acute invagination operation should be performed as soon as possible after properly employed non-operative measures have been tried without success. When a laparotomy has been done, disinvagination is to be preferred when it can be carried out without special difficulty. If the intestinal wall at any place in the area of invagination is suspicious, a strip of iodoform gauze should be introduced to this place or the affected area excluded from the abdominal cavity. Resection of the whole invagination is indicated when the intestinal wall shows marked changes or threatens perforation. The employment of an artificial anus, or enteroanastomosis, is to be condemned. The author believes that in ileocecal and colon invagination, when disinvagination has been difficult and the serous surface of the intussuscipiens is intact, the intussusceptum may be resected. In case, however, the invagination is only a short one, a total resection should be done, because of the better prospects of a radical cure, although one should also take into account the general condition and age of the patient. If very short, unless reduced with very little difficulty, resection is to be preferred to all other methods. But even when the invagination is easily reduced, a secondary resection must be kept in mind, since it is the only sure means for the prevention of a recurrence. Haagn (Deut. Zeit. f. Chir., S. 142, 1911).

Sigmoidectomy.—As the sigmoid flexure is a favorite seat for cancerous

growths it is often necessary to excise this portion of the bowel. In some cases no attempt is made to restore the continuity of the bowel, but the operation is terminated by forming an artificial anus. If, however, the sigmoid is movable and the tumor can be removed cleanly, an end-to-end anastomosis may be made. Even when the rectum needs removal with the sigmoid, operators have preferred to draw down the sound intestine and suture it to the anal region.

SURGICAL AFFECTIONS OF THE PANCREAS.—These comprise inflammation, cancer, cysts and calculi. There are no typical operations for these affections, or upon the pancreas and its duct for any conditions.

> The most important and special indications for operative interference in morbid states of the pancreas are: 1. Injuries to the pancreas from stab or bullet wounds, or severe contusions in the epigastric region. 2. Inflammations —(*a*) acute hemorrhagic pancreatitis; (*b*) subacute pancreatitis; (*c*) chronic pancreatitis. 3. Pancreatic cysts. McReynolds (Wash. Med. Annals, May, 1908).

Acute Pancreatitis.—In this condition the pancreatic juice escapes into the tissues of the pancreas and into the peritoneal cavity, and the effect of its irritating influence is very destructive. The reddish, purulent fluid in the vicinity can be removed by a drain, and tense parts of the pancreas can be scarified to allow some of the interstitial exudates of the pancreas to drain out. Drainage is essential after removing tumors, or after an injury to the pancreas in order to dispose of the irritating pancreatic secretion.

The escape of pancreatic secretion from an injured gland reduces living fat in this vicinity into its fatty acid and glycerin, due to a ferment in the pancreatic fluid. The glycerin is absorbed and the fatty acid which remains makes a combination with lime salts, with the effect of producing small areas of dull white at points where the reaction has taken place.

Acute pancreatitis should be the occasion for prompt abdominal section for the severe and fulminating symptoms usually present, and emergency laparotomy would in any case be required. If the patients have not died outright of collapse or peritonitis, the fat necrosis or some other secondary condition will demand operation.

> Report on diagnostic value of Cammidge reaction based on 504 examinations. Of 26 patients who were shown to have pancreatitis, only 9 (35 per cent.) gave a positive reaction, and, even of these, 7, in one or more of the series of 3 tests, gave negative results. Of the 74 sick persons without pancreatitis, 35 (47 per cent.) gave one or more positive reactions. Of the 207 sick persons who, in all probability, had no pancreatitis, 73 (35 per cent.) were positive. Of the 17 well persons, 5 (30 per cent.) were positive. Even when the most elaborate care is exercised to follow the technique of Mr. Cammidge's "C" reaction, in the most uniform manner, *if knowledge of the clinical histories and other factors of the personal equation be eliminated,* the end results, judged by Mr. Cammidge's own criteria, must be considered, as a means of diagnosticating disease of the pancreas, as both valueless and misleading. Wilson (Surg., Gynec., and Obstet., Aug., 1910).
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> Report on diagnostic value of Cammidge test as studied in dogs. The Cammidge test is of little value in establishing the diagnosis of acute pancreatitis in dogs. If the test is negative, it is pretty strong evidence against an acute pancreatitis. It is of even less

value in the condition of chronic pancreatitis in dogs and may be consistently absent, even in extreme grades of this disease. A positive Cammidge test is not infrequent in normal dogs and men. The Cammidge test is almost constantly present in chloroform poisoning in dogs—a condition in which there is extreme liver necrosis and cell autolysis. It may be present in cases of pneumonia, or in any condition where there is active cell destruction and autolysis. It may be produced experimentally almost at will by intraperitoneal injections of hydrolytic cleavage products. These split products may be prepared by boiling pneumonic lung-tissue (dog or man), or thymus, for hours with dilute acid, neutralizing, filtering, and concentrating to a clear fluid. Whipple Chaffee and Fisher (Johns Hopkins Hosp. Bull., Nov., 1910).

The pancreas may be reached either above or below the stomach, through a second incision into the omentum or mesocolon, after making a suitable external incision. A counteropening through the lumbar region may be necessary for drainage. If an abscess is still intact it should be opened wherever most accessible. The infrequency, fatal character, and operative mortality (chiefly unavoidable) do not justify us in devoting much space to abscess of the pancreas, the treatment of which largely resolves itself into management of the secondary conditions to which it gives rise. Shallow incisions followed by simple wick drainage carried to the pancreas certainly serve to remove poisonous exudates to advantage in some cases of acute pancreatitis, and even the simple use of wick drains without scarification of the pancreas is sometimes followed by good results. We must leave room when draining to allow necrotic masses to escape.

In acute hemorrhagic pancreatitis the gravity of the affection is due to the necrotic destruction of the pancreas rather than to the hemorrhage. Chronic pancreatitis consecutive to gall-stones is a well-individualized morbid entity, and the cure after effectual drainage of the bile passages proves its dependence on the lithiasis. The operation is more successful the earlier it is done, before glycosuria reveals disturbance in the internal secretion. Cappelli (Policlinico, Aug., 1909, Surg. Sect.).

Cancer.—A radical operation for cancer of the pancreas is hardly to be considered, and the only palliative procedure recognized is done for the relief of obstruction of the intestine or bile-tract.

Cysts.—As a rule these can only be dealt with by incision and drainage. In a few cases small encysted collections of fluid affecting only a portion of the organ have been excised outright. In a few other cases cysts have first been opened and drained and then excised as a subsequent stage of procedure.

Report of 16 operated cases: 2 of pancreatic cyst, 1 of pancreatic carcinoma, 3 of acute purulent and 5 of chronic pancreatitis, and 5 of hemorrhages into the pancreas. The writer cautions against exploratory punctures for diagnostic purposes, and emphasizes the impossibility of differentiating between pancreatitic cancer and chronic pancreatitis. Necrosis of the pancreas may be the result of inflammation or hemorrhage, while fat necrosis is due to the escape of pancreatic secretion into the intra-acinous structures, this occurring most frequently after hemorrhage, and less often after pancreatitis. Of the 5 cases in which operation was done for hemorrhage, 1 recovered because the condition was recognized early and surgical intervention was promptly resorted to. Bode (Beiträge z. klin. Chir., Bd. lxxi, Hft. 3, 1911).

Calculi.—When, as occasionally happens, the pancreatic duct is obstructed by a calculus the condition cannot be diagnosticated readily, but is recognized when operating for some other condition, usually for gall-stones. A pancreatic calculus may sometimes be distinguished from a gall-stone with the fluoroscope. The indication is then the same as in obstruction of the common duct.

One of the few surgeons who have discussed typical pancreatic operations is Villan, but it is not easy to determine what, if any, portion of the work he describes has been done on the living human being. For those interested we append a synopsis of his work.

Villan considers the surgical management of pancreatic diseases as well as the typical operations, but it is doubtful if any of the latter have attained sufficient dignity to be thus regarded.

The term pancreatotomy is applied to incision of any portion of the organ or its surrounding tissues, for any purpose. If followed by suture it is termed pancreatorrhaphy. Pancreatostomy or fistulation of the pancreas is simply pancreatotomy with drainage, and is a frequent procedure in the surgical treatment of cysts, abscesses, etc. Pancreatectomy, partial or total excision, is used chiefly in tumors of the organ (and in traumatisms and connection). These operations will be considered elsewhere in detail. Pancreaticotomy, pancreaticostomy, and pancreatic anastomoses will also be considered in detail.

Pancreatectomy.—This is necessarily partial. It has been done only to the extent of excising tumors. The tumor must first be freed from any attachment to neighboring organs as well as from the pancreas itself. The *excision of the tail of the pancreas* is attended with much less danger. The tumors here are more likely to be pedunculated. Median laparotomy is followed by liberation of the tumor, traction and application of strong forceps or ligatures, which prevent the entry of blood and pancreatic juice into the peritoneal cavity. The pedicle is then divided and cut and sutured, peritoneum sutured, and wound closed. It is often prudent to tampon and drain. Excision of the head of the pancreas is difficult and dangerous. Either a part or the whole may require removal. The tumor is detached with scissors and bleeding vessels ligated. The ducts of Wirsung and Santorini should be left intact, although the preservation of either one will suffice.

If Wirsung's duct should be divided it is usually sutured, and the same is true of the common bile-duct should it be injured, although atmospheric pressure will sometimes serve to restore continuity of wound margins well enough. The operation is finished by suturing the remains of the pancreas to the duodenum.

If the entire head of the pancreas is to be extirpated, it is necessary first to ligate the pancreatic duodenal artery and the right gastroepiploic. The duodenum must not be separated from the superior mesenteric artery. Wirsung's duct and the common duct must be kept intact when possible; otherwise they must be preserved by anastomosis.

The entire pancreas can hardly be excised as a routine procedure, although the operation may be suc-

cessfully performed on animals and even man. It is followed by diabetes mellitus.

> Case of resection of part of the pancreas; approximately two-thirds of the gland was replaced by the tumor. The results of the experimental work done by Halsted, Flexner, Opie, and Coffey in this country, and abroad by Pawlow, Biondi, Desjardins, Robson, and a host of others, may be summed up as follows: Total pancreatectomy is followed in a short time by the death of the animal. Partial pancreatectomy, on the other hand, permits of an indefinite existence, compensatory regeneration and hypertrophy not infrequently taking place.
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> In properly selected cases and under favorable conditions, followed by careful protection of the field of operation by peritoneum and provision for the escape of the pancreatic secretion by ample gauze drainage, operations involving resection and suture of the pancreas were followed by surprisingly good results. J. M. T. Finney (Annals of Surg., June, 1910).

Pancreaticotomy.—This operation consists in incising the pancreatic duct for calculi. The duct, as in the corresponding operation on the common bile-duct, may be approached directly or through the duodenum.

Simple Pancreaticotomy.—After laparotomy and exploration, if a calculus is found therein, the canal is incised, and the concrements removed by forceps or other apparatus designed for the purpose. Suturing of the cut duct is not necessary. A fistula naturally remains (pancreaticostomy), but has a tendency to close spontaneously.

Transduodenal Pancreaticotomy.—The duodenum is lifted upward. Incision should be made in the anterior portion, and while some surgeons advocate a transverse, others prefer a horizontal incision. The ampulla of Vater should now be located, and if a pancreatic stone is present the opening may be incised in order to extract it. Suture of the incision is not necessary.

Cathetering of the pancreatic duct and crushing of large calculi are recent procedures in connection with this operation.

Pancreaticostomy and pancreaticoenterostomy have been done very extensively in animal experiment. In human surgery, incision of the pancreatic duct with drainage has been practised, but the operation of pancreaticoenterostomy, which conserves the pancreatic juice in the intestine, is much more rational, and in several instances anastomoses have been effected between the canal of Wirsung and some part of the digestive tract.

The pancreaticoduodenal region is exposed as for pancreaticotomy. Sutures or Murphy's button may be used. The dilated duct should be freed from adhesions and either grafted into the intestine or, what is preferable, a lateral anastomosis may be made. Pancreatic fluid coming in contact with the other tissues may cause local or distant necroses.

SURGICAL AFFECTIONS OF THE SPLEEN.—Abscess.—Splenic and perisplenic abscess will in all likelihood end fatally unless some unusual path is taken by the burrowing pus. Incision and drainage is the usual procedure, but, if the spleen is freely movable or readily freed from adhesions, splenectomy may be the indication of choice.

Cysts.—Simple and parasitic cysts of the spleen are best treated by incision and drainage in the same way as

we treat abscesses. If the spleen is not bound down by adhesions, the operation may be done more safely as a two-stage procedure, the first of which consists in suturing the cyst wall to the abdominal parietes without opening of the former, and waiting for forty-eight hours for the formation of protecting adhesions.

Splenomegaly. — Enlarged spleen from whatever cause is usually left to medical resources, unless it becomes so large as to cause serious pressure symptoms, in which case removal of the spleen may become a necessity.

Floating Spleen.—While splenopexy has been sometimes done for this condition, most operators prefer the more radical removal of the spleen because of the difficulty of holding this organ with sutures, due to its friable tissues. The spleen may be fixed through an incision made obliquely along the left costal margin to the quadratus lumborum muscle. The patient is placed in the abdominal position upon a pad or air cushion similar to that used for forcing the kidneys against the abdominal wall. The peritoneal surface of the spleen is scarified, and so is the corresponding peritoneum of the abdominal wall. Kangaroo-tendon interrupted sutures entered at the lowest margin of the spleen serve to fasten it nearly in normal position, and a packing of gauze with a protecting apron of gutta-percha tissue gives support until supporting adhesions have formed. Rydygier, for fixing the spleen, makes an incision in the middle line of the abdomen high up, and forms a pocket in the parietal peritoneum through a transverse peritoneal incision, and then with the fingers forms a pouch, into which the lower half of the spleen fits. The spleen is secured in this pouch by a few points of suture.

Neoplasms.—Solid tumors of all kinds and tuberculosis require early removal of the spleen.

TYPICAL OPERATION OF THE SPLEEN.—Splenectomy.—The typical external incision is median in traumatic cases (not considered here), but in all others either the semilunar line or one following the costal arch at a distance of an inch or so gives better access to the pedicle. The next stage is purely exploratory and involves division of peritoneum and examination for adhesions. If there are no diaphragmatic or pancreatic adhesions, it is usually possible to isolate the organ, although extensive ligation may be required. It is sometimes necessary to free the spleen from the pancreas by sacrificing a portion of the latter. The organ is then lifted out of the wound, and packed about with gauze. It must be remembered that the spleen is very easily wounded before it can be ligated off, and that profuse parenchymatous oozing will then delay the operation. As in other operations on abdominal viscera, traction on the pedicle may induce shock, because of the intimate connection with the solar plexus.

The next stage consists in ligating the spleen vessels, which is accomplished by tying off the splenorenal ligaments and gastrosplenic omentum and ligation of the vessels of the hilum. The latter is naturally the ideal choice, but the delay involved adds to the dangers of shock, and unless the patient is in sound condition to withstand operation it may be advisable to transfix the pedicle in one or two planes according to its

width, and ligate each by itself. It is well to have apparatus ready for intravenous infusion, which may be begun at any moment that danger from hemorrhage appears.

The after-treatment calls for no special principles. When the danger from hemorrhage or sepsis appears to be slight, the external wound may be closed at once.

The position of the patient during operation is important. A large sand-bag should be placed under the back, under the upper end of the spleen, and the foot of the table lowered about six inches. The incision may be median or through the left rectus muscle, preferably the latter. It should be ample, and, if necessary, a transverse incision may be made from the upper end of the primary wound parallel to and half an inch below the lower border of the ribs.

The splenophrenic ligament should be first attacked. The operator, covering the spleen with gauze, draws it to the right, while an assistant draws the left lip of the wound to the left. Where possible, the splenic ligaments and all vascular adhesions should be doubly ligated in sections and cut between the ligatures; but when this is difficult the ligaments may all be clamped and the blood-supply entirely cut off in this way. The spleen may then be removed and the clamps afterward sewed round and removed as in oöphorectomy. In difficult cases with extensive adhesions it is possible to grasp all the gastrosplenic ligament between the index and middle fingers of the left hand and to apply a long, curved, rubber-covered clamp. After securing this ligament first, the other ligaments may then be clamped or ligated and cut, after which adhesions may be rapidly separated and the bleeding controlled by gauze packing. Carr (New York Med. Jour., Feb. 16, 1907).

When a spleen is removed in a case in which there is not a splenic leukemia of advanced character, the operation is quite as safe as is the one for removal of the thyroid or of the uterus or any other simple operation, provided that the same systematic plan is followed. There should be no severe traction on the pedicle of the spleen or great manipulation of the veins, because they are exceedingly friable. After severing the pedicle below, care should be taken to protect the smaller veins which often enter the spleen from above. If one is careless, one will find that some of the large veins which pass through the accessory ligament are exceedingly troublesome, but when these things are looked after in patients not suffering from splenic leukemia the operation is a safe one. The author has had one of these patients go through a severe pneumonia afterward under the care of one of our best internists, who found no difference whatever in the course of the disease. If the leucocytosis is higher than 50,000, then one can count on a fatal hemorrhage after the splenectomy. The writer states that his experience in 15 or 20 cases is not sufficient to be of any value except as a guide. If there is leucocytosis accompanied by a rise in temperature, then, of course, there is no occasion for the operation, because one would no more operate in this chronic condition while there is an acute infectious condition present than for any other chronic surgical condition. Therefore, if the leucocytosis is the result of the leukemia, one must be guarded in the operation, and not fear hemorrhage from the large vessels at all, but hemorrhage from the small adhesions. The blood will continue to ooze out. Gauze may be sutured over the surface, and the blood will ooze out of the stitch holes. It will ooze out, no matter what one does in these cases of advanced splenic leukemia. A. J. Ochsner (Jour. Amer. Med. Assoc., Jan. 1, 1910).

The writer usually uses an incision through the left semilunar line, carrying, if necessary, the upper end along the costal margin to the ensiform cartilage. He has not found Myer's procedure of cutting the costal cartilages

necessary as yet, but in some cases a left transversal incision joining the longitudinal is convenient. In advanced disease, adhesions, especially to the diaphragm, are occasionally difficult to separate until after the splenic pedicle has been secured. To grasp this vascular pedicle temporarily in rubber-covered elastic clamps is the most important step in the operation if the vessels are fairly sound. This must be very carefully done on account of the delicacy of the splenic veins. To grasp the pedicle securely the organ should be turned over, at least enough to grasp the vessels in the hand. With the fingers and blunt dissection, a passage is made around the pedicle and a clamp applied and tightened enough to control the circulation until the spleen can be entirely separated and delivered outside the wound. If extirpation is the object of the operation the pedicle can be secured at any time after the application of the elastic clamp, which is applied as close to the root as possible, so as to leave distal to it ample space for ligation. If partial resection is to be done, temporary compression of the pedicle seems harmless if there are no gross vessel-wall changes, and after the use of the clamp the desired amount can be resected and the hemorrhage controlled by buttonhole catgut suturing with a round needle, as in liver resection. "It has been shown experimentally that reduction of the artificial supply by ligation results in atrophy of the spleen, and, so long as the veins are left intact, necrosis does not occur. If the splenic artery divides in the hilum, ligation of branches would appear to be an active competitor of partial splenectomy. We have not found the marked alterations in the walls of the blood-vessels which have been shown to be often present at *post mortem,* and which probably represent a terminal condition." W. J. Mayo (Jour. Amer. Med. Assoc., Jan. 1, 1910).

Four cases of splenectomy upon malarial spleens. The first case was operated upon four and a half hours after rupture of the enlarged spleen by injury. The patient died a few hours after operation, primarily from the hemorrhage which followed the rupture. The remaining 3 cases recovered from the operation with much improved health, and have remained free from the malarial paroxysms to which they had been subject. Statistics of this operation show that in 24 cases collected by Bessel-Hagen up to 1890 the mortality was 65 per cent., while in 64 cases operated upon in the following decade it was 25 per cent. Solieri (Archiv für klin. Chir., Bd. 92, Hft. 2, 1910).

SURGICAL DISEASES OF THE LIVER AND BILIARY PASSAGES.—The chief occasion for surgical intervention in these localities is gall-stone disease and its numerous consequences, for the relief of which typical operations are required. Surgical affections of the liver proper, while numerous, are less frequent, and for the most part are relieved by simple general procedures, as incision and drainage.

Abscess of the Liver.—Here may be considered abscess of the liver proper, and suppurative pericystitis. As soon as the diagnosis is made the pus should be drawn off with an aspirating apparatus, and most surgeons prefer to make an exploratory incision for this purpose. In some cases it may be necessary to excise one or more ribs and go through the pleura, in which case the operation should consist of two stages in order to allow protective adhesions to form. After the pus has been removed an incision should be made of such character as to insure complete drainage, and the abscess cavity allowed to close. If much liver tissue has to be divided to expose the abscess cavity, it will be necessary to use the cautery for hemostasis.

Subphrenic abscess may be considered here, although it may occur

on the left side and have no connection with the liver. The general principles of operation here are the same as in abscess of the liver—exploration, aspiration, and eventually incision and drainage. It may be necessary to go through the thoracic wall.

Cysts of the Liver.—Hydatids should be extirpated if possible, the operation amounting to hepatectomy, which see. So radical a procedure is seldom carried out, and the usual intervention, both for hydatids and non-parasitic cysts, is incision and drainage, with the possibility of going through the thoracic wall. The operation may be done in two stages with an interval for the formation of adhesions, or it may be done in a single sitting, the cyst being sutured to the operation wound before incision.

Neoplasms.—A single focus of primary cancer may sometimes be removed by hepatectomy; sarcoma is inoperable.

Cirrhosis.—This has been considered under Ascites (Surgery of Peritoneum).

Hepatoptosis.—Hepatopexy is done usually in conjunction with other operations. The liver is scarified or brushed on the cephalad surface, and one of several methods in addition for retaining it *in situ* are essayed. The author includes shortening of the suspensory ligament.

Cholelithiasis.—Simple accumulation of gall-stones, apart from the complication and secondary mischief, demands surgical removal. The choice then lies between cholecystostomy and cholecystectomy.

Cholecystitis.—When the gall-bladder has become chronically inflamed, altered by disease and adhesions, it should be extirpated. Partial cholecystectomy is not looked upon with favor. If the process is relatively mild, with the ducts free and intact, cholecystostomy may suffice, but, like the appendix, a gall-bladder once infected is always infected.

Obliteration of Bile-passages from Without.—This is most commonly due to cancer, but may be due to other tumors and inflammatory processes. The typical operation for obstruction from without is an anastomosis between gall-bladder and intestine (cholecystenterostomy). When this is contraindicated permanent drainage by a biliary fistula (cholecystostomy) is the only resort.

TYPICAL OPERATIONS ON BILIARY PASSAGES AND LIVER.—These are few in number, viz., cystostomy, cystectomy, and choledochotomy, cholecystenterostomy, excision of liver. Other operative procedures appear to necessitate only general principles, such as exploratory laparotomy, evacuation of pus, etc. The typical operations on the biliary passages are performed for cholelithiasis, incidentally including chronic cholecystitis.

Analysis of 350 operative gall-bladder cases, derived mainly from material furnished by A. J. Ochsner. Where the benefit derived from the operation has not been unquestionable the result is stated as unimproved. In 245 cases where gall-stones were found, 79 per cent. report themselves entirely cured by the operation and 6 per cent. consider themselves as cured though still suffering from minor discomforts. This gives 85 per cent. good results. Twenty-one, or 9 per cent., are classed as improved, and 15, or 6 per cent., as doubtful. The writer's conclusions are as follows: 1. In the hands of those qualified to undertake the work, the

operative treatment of gall-stone disease is one of the most satisfactory branches of surgery, and the cures may be safely estimated at over 80 per cent., while the majority of the remainder are so much benefited as to justify the operation. 2. The most favorable cases in all respects are those in which the stones are still confined to the gall-bladder. The operative mortality in these uncomplicated cases is almost *nil*, and the proven end results are practically all that could be desired. These two facts in themselves should enable us to settle any question as to the proper time for operation. 3. The most important principle of gall-stone surgery is the complete removal of the stones, with the least possible damage to the biliary tract. Overlooked stones are probably the most important simple cause of uncured patients. 4. If, as a result of the operation, all obstructions within the biliary tract are removed, a cure is almost certain to result. No evidence has been found in this series of cases to show that cholecystectomy should ever be the operation of choice in gall-stone cases, unless there be chronic cystic duct obstruction or the gall-bladder so diseased as to make a cholecystectomy technically safer and easier to perform than a cholecystostomy. 5. Every effort should be made to guard against postoperative hernia. 6. A guarded prognosis should be given in cases complicated by pelvic lesions. 7. In our series, cases of cholecystitis without stones have not shown better results than could probably have been attained by medical means, and unless better results are attained in this class of cases in the future surgeons should learn to avoid them. E. M. Stanton (Jour. Amer. Med. Assoc., Aug. 5, 1911).

Simple Cystotomy.—The gall-bladder, having been exposed, is incised between two toothed forceps, and the stones if present removed with finger or blunt curet, taking care to remove all possible concrements, some of which may lie close to or in the opening of the cystic duct. One finger should be applied along the bladder externally, to aid in localizing concrements. Folds and diverticula resulting from cholecystitis may contain concrements. The cystic duct and common duct must be palpated and, if stones are contained therein, choledochotomy may be required. The author prefers amputation of the greater part of the gall-bladder as a rule, because it removes an infected structure and avoids the distress caused by the lower margin of the liver impinging upon a gall-bladder sutured to the abdominal wall.

Cystostomy.—Cystostomy with Drainage.—This form of cystostomy is really then a partial cystectomy. The tube remains in position eight or ten days, the bile escaping freely. After the tube has been withdrawn, a little bile may escape up to a week or so longer. As a rule, these fistulæ close spontaneously without trouble.

Cystectomy.—Surgeons have proved by experience that cystostomy had many drawbacks. It is the conservative method, but leaves behind a diseased gall-bladder, which invites new surgical disorders. Adhesions which are invariably present cause the organ to lose its mobility, thus increasing the liability to further infection. Cystectomy, an operation originally performed only on suspicion of cancer, has been the choice of the author for some years, the suggestion having come from Langenbeck's discovery of the safety of extirpation of the organ originally, and this idea confirmed by many operators later.

Excepting in cases of cancer the author prefers the same operation for cystectomy that he does for cys-

tostomy, for the reason that the small portion of gall-bladder which is allowed to remain allows of easier fastening to the drainage tube, and lessens the annoyance of hemorrhage from the artery and vein of the cystic duct.

Technique.—The gall-bladder, having been exposed, is freed from adhesions and from the normal peritoneal reflection to the surface of the liver. The presence or absence of gall-stones in the bladder is only of incidental importance, because it is for infection of the gall-bladder that the operation is done. The freed gall-bladder can be handled very much as one would handle the appendix, and the operation from this stage on is somewhat similar. Any bile or concretions which are found in the lower part of the gall-bladder or the cystic duct are stripped out with the fingers into the cavity of the gall-bladder proper, which remains unopened. The part which has been emptied by stripping with the fingers is then ligated or clamped with a pair of forceps to prevent the return of contents to the region of the operation. A longitudinal incision large enough to allow the entrance of a small soft-rubber catheter is then made below the clamp or ligature, and extending as far as or into the lumen of the cystic duct. The catheter is introduced into this opening and tied in place with a catgut suture piercing the wall of the cystic duct and catheter alike. This avoids displacement caused by vomiting. The next step consists in tying another catgut suture snugly around the cystic duct or the lower portion of the gall-bladder so firmly as to cut off all circulation in the walls. The gall-bladder is then amputated between the clamp and ligature, and the lumen of the stump at the point of compression by the ligature may be sterilized like the stump of the appendix, by brushing it with 95 per cent. carbolic acid neutralized a moment later with alcohol. The catheter, acting as a drainage tube, is then left escaping from any convenient angle of the wound of the abdominal wall. In two or three days the constricting suture is usually absorbed and the flow of bile then begins through the tube, which can be removed at any time subsequently, because the suture of catgut fastening the catheter to the cystic duct is absorbed at the same time with the constricting suture. The advantage of this technique is that peritoneal adhesions have had time to wall in the area of operation so that bile or septic fluid escaping from the region of the stump makes its way safely to the surface. Sometimes it is an advantage to split the catheter longitudinally throughout its entire length, and to lay a strand of gauze loosely in the catheter because this gives us capillary attraction to help in guiding bile or septic fluid to the surface; and if the walls of the catheter are prevented from closing entirely, any blood or other fluid between the stump and the external incision is drawn out the same way by capillarity.

Some surgeons do not consider partial excision as a typical operation. They state that cases occur in which the gall-bladder is so fragile that its liberation would be impossible, but such cases make a small part of the ones actually dealt with in practice, and practically the same principles can be observed.

The writer's only contraindications to cholecystectomy are: 1. Grave complicating diseases, *e.g.*, typhoid fever. Even in the latter, he advocates subsequent removal of the gall-bladder to prevent as far as possible the patient becoming a typhoid carrier. 2. Complete obstructive jaundice. A second-stage removal of the gall-bladder is also indicated here, especially if the patient has signs of hepatic cirrhosis. 3. In aged or feeble patients and in those who take the anesthetic badly, so as to save time and shock. H. Lilienthal (N. Y. Med. Jour., July 1, 1911).

Choledochotomy.—This operation comes into play when after cystectomy the common duct or the hepatic duct is found diseased or containing concrements. A wide external incision is requisite when it is believed that this operation is indicated. Exposure may be difficult on account of the conformation of the thorax, or when adiposity interferes. It may be necessary in such cases for an assistant to draw aside all the surrounding viscera widely with the hands, with gauze beneath the fingers. If adhesions are absent the common duct may be lifted into the field with the fingers or a pair of padded forceps. The peritoneal covering is slit. The large vessels—hepatic artery and portal vein—behind the biliary passages are to be avoided. A small vessel running obliquely across these must be held aside or tied and divided. Two lymph-glands in this locality may be so enlarged and inflamed as to simulate concrements. The common duct must now be examined for concrements and inflammation. If concrements are palpable, the duct is opened between slipnooses or forceps. Bile will at once escape and must be caught up with gauze pledgets and the stones, if present, removed with small forceps or curets.

As a rule, however, extensive adhesions are present, and the operation is much more complicated. These adhesions must be separated as far as possible, and if the cystic duct has not already been opened it should be incised. If the object were not primarily to extirpate the gall-bladder, this should now be done and the cystic duct divided. The choledochus should next be sounded through the opening, the finger palpating the outside of the canal. If concrements are present, the cystic duct may be laid open slowly until the common duct is reached. By the aid of small curets and forceps, and palpation externally, small concrements may be extracted. If necessary the incision may be continued into the common duct as far as the duodenum. Extraction of stones from an inflamed or dilated choledochus requires the same precautions as in the case of the gall-bladder. That portion of the duct behind the duodenum is very difficult of access, unless the reflection of peritoneum from the duodenum is first cut away. In cases of this sort it has been necessary to enter the duodenum.

The conservative method is to draw the duodenum to one side after freeing the peritoneum, but this is believed by some to affect the nutrition of the latter unfavorably. A drainage tube is inserted into the choledochus, and the latter sutured up to the tube by most operators, but the author usually dispenses with sutures, excepting the single one for holding the tube in place, because the walls of the duct normally fall together well, and atmospheric pres-

sure keeps the cut margins together as well as sutures would do it, unless much unusual injury has been caused by the operative work.

Case of bile fistula in which it was not possible to utilize the hepatic duct for drainage; the writer consequently sutured the duodenum directly to the main intrahepatic biliary duct. Doberer (Wiener klin. Woch., Oct. 13, 1910).

Cholecystenterostomy.—A typical operation indicated is closure of the biliary passages from without. A long abdominal incision is required, oblique or angular, beginning at the ensiform cartilage and carried down through the right rectus muscle. The intestines are controlled by gauze. If gall-stones are present they are removed, and it must also be determined that suspected cancer of the pancreas is not a calculus in the pancreatic region. A choice of intestinal locality for anastomosis is then in order.

The duodenum is the ideal region, but in practice a high jejunal anastomosis is often preferable. The gall-bladder is emptied upon gauze, and the apex seized with a clamp. A loop of jejunum is similarly held with the fingers. Both structures are opened to the extent of a finger-tip, as in gastroenterostomy, and the suture is also performed as in the latter. This locality may be fortified with omentum, if the operator wishes.

The Murphy button is useful for this anastomosis and is used by many operators, but simple suture suffices for most cases.

Excision of Liver; Hepatectomy.—Indicated in tumors chiefly, including cysts, and sometimes after traumatisms. When a pedicle is present or the mass occupies the margin of the liver, hepatectomy is very easily performed by the aid of ligation.

When this is impossible the mass is removed step by step, followed by ligation of all bleeding vessels. It is often possible to ligate these in advance of division with a needle armed with catgut. After extirpation it is in order to ligate all lumina of blood-vessels with the aid of a needle rather than with forceps, and then suture the liver with catgut. Buried sutures are undesirable for the liver, however, as blood and bile seep into them. Pressure may be brought to bear for controlling hemorrhage that is not from spouting vessels, in some cases. Pressure is obtained by carrying a long catgut ligature deeply through the wound in the liver, and fastening each end of catgut to a broad plate of sheet lead. If the entering end of catgut is first fastened to its respective plate of lead, the emerging end of catgut can be tightened to any desirable extent before fastening it to the second lead plate. Ears fashioned on the lead plates can be bent over to hold the catgut ends, and silk strands fastened to the plates and led out of the wound serve for removing the plates eventually when the catgut is absorbed. More than one pair of plates may be used for an extensive liver wound.

Extensive resections of the liver can be carried out with the most simple means. If care is taken not to stretch the vessels in cutting through the liver and not to pull them out, it is not difficult to apply hemostatic forceps and to apply a ligature, while the vessels which are cut obliquely have to be taken care of by circular suture. Compression suture of the wound in the liver and catgut suture of the surface are the safest means of hemostasis. It is best to press together two wounded

surfaces of the liver by suture, and, therefore, whenever possible, to make the resection in the shape of a wedge placed in an approximately vertical direction to the margin of the organ. Garre (Surg., Gynec. and Obstet., Sept., 1907).

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ABDOMINAL INJURIES.—Under this heading will be considered the broad field of injuries of external origin to which the abdomen and the abdominal viscera are liable. These include *contusions,* which are important mainly because of the lesions to which the intra-abdominal organs are exposed; *non-penetrating wounds,* in which the abdominal walls alone are injured, and *penetrating wounds,* in which the walls and the abdominal viscera are penetrated.

CONTUSION OF THE ABDOMEN.—SYMPTOMS.—Whether caused by blows, kicks, spent bullets, the passage of heavy bodies—such as vehicles—over the abdomen, etc., the symptoms attending a contusion in this region are not always such as to call attention to the seriousness of the lesion present. The gravest abdominal injuries may coexist with practically no external or general indication of mischief, the patient walking a long distance, perhaps, without experiencing anything more than slight local pain where the blow had been received.

Case of patient run over by a milk wagon, in which no serious disturbance manifested itself until about eleven weeks after the injury occurred. The patient then noticed a lump about the size of a hen's egg near McBurney's point. Two weeks later the swelling ruptured and some pus was discharged. The mass consisted of suppurating omentum, with partial rupture of the aponeuroses of the external oblique and a localized rupture of the muscular portion of the internal oblique and transversalis muscles. Recovery followed suitable treatment. Kahlke (Surg., Gynec. and Obstet., Feb., 1907).

Intestinal lesions produced by blunt force are most frequently encountered in males during youth and early manhood, and in females during childhood, these, of course, being the periods of greatest exposure to trauma. Pre-existing lesions, such as hernias, ulcers, adhesions, etc., increase the liability of rupture should trauma occur. Lax abdominal muscles afford less protection than a wall which is contracted, and hence very sudden accidents are more frequently the cause of visceral lesion than those in which the patient has some warning. All parts of the gastro-intestinal tract have been injured, to say nothing of the other abdominal viscera, but the ileum and jejunum are more often involved, the colon and stomach less frequently. Thus in 219 cases, the small intestine was affected 172 times, the large 26 times, and the stomach only 21 times. That vomiting is apt to arise sooner if the lesion be above the level of the umbilicus than if it be below is probable. Stone (Annals of Surg., Sept., 1910).

In all injuries of the abdominal viscera without external lesions careful examination is necessary and continuance of the observation kept up over a period of several days or more. No matter how slight the symptoms referable to the abdomen, the possibility of visceral injury must be considered, regardless of the point of injury or the external force employed. The degree of violence has often no relation to the extent or severity of the injury to the internal organs, and an investigation as to the exact details of the accident or violence is essential for the diagnosis. Blows, kicks, and crushing violence cause most of the intestinal injuries; compressive force is the most common cause of liver trauma, and concussion is responsible for most of the splenic ruptures. The presence or absence of

peristalsis is of the utmost diagnostic and prognostic importance and has not been duly appreciated. The early presence of a peristalsis indicates that the abdomen or its contents have received some shock or violence, and its persistence or recurrence is a conclusive proof of internal or visceral injury. Any decided lessening of peristalsis is a danger signal if it occurs more than three or four hours after the injury. Active peristalsis, on the other hand, is always encouraging. There are no pathognomonic symptoms of abdominal injuries, most of them being common to all injuries, but, in general, progressively increasing shock indicates trauma of the solid organs, while early symptoms of peritonitis follow that of the stomach or intestines. Pain as an initial symptom is important only as calling attention to the fact that an injury may have occurred and, possibly, by its location, showing the possible site of the injury. Shock has no diagnostic value except by its progress or course, which is of great importance. H. H. Sherk (Jour. Amer. Med. Assoc., March, 1911).

Although the abdominal walls may be but slightly injured, the lesions may consist of extensive extravasations of blood between the layers, or sufficient laceration of the muscular and other tissues to give rise to more or less local sloughing. Such lesions of the abdominal wall, however, are not always accompanied by injury of the abdominal organs.

Usually, in these cases, according to Scudder, the greater the force the greater the injury, but a trivial blow may result in serious damage to intra-abdominal viscera. A hollow organ, if distended, is more vulnerable than if empty. Inquiry should be made as to the last mealtime and as to the last micturition. The exact direction of the blow is important. The clothes of the patient sometimes offer some indication as to the injury.

A trifling superficial injury of the abdominal wall may be associated with serious internal lesions, owing to the resistance offered by the abdominal walls and the fragility of the abdominal organs. The external appearances, therefore, should not be taken as a criterion.

From observations of some twenty cases of visceral injury, following contusion of the abdomen, verified by operation or autopsy by Brewer, the most prominent were pain, tenderness and muscular rigidity, and likewise the most reliable. The deep-seated, localized pain following injury, especially increased by pressure, and accompanying local or general muscular rigidity, is one of the most constant signs of intra-abdominal injury. Brewer holds that the association of these three symptoms is almost pathognomonic of abdominal irritation. Pain, however, is often present, with tenderness, in injuries limited to the abdominal wall; but in these instances muscular rigidity is generally absent. In the absence of subcutaneous pain localized tenderness with rigidity is strongly suggestive of visceral injury. Of the three symptoms, muscular rigidity is the most reliable, and sometimes the only sign. In the absence of other diseased conditions spasm of one or more of the abdominal muscles following the traumatism may be looked upon as nature's effort to protect an injured organ from further irritation. Vomiting is a symptom often present, but not always an accompaniment of severe visceral injury. It is commonly present with involvement of the stomach and upper part of the intestinal tube, and with injuries resulting in severe shock. The signs

of free fluid in the abdominal cavity are very suggestive.

In most cases, however, severe contusions of the abdominal wall, whether the deep organs are involved or not, are followed by agonizing pain in the region of the injury, restlessness, nausea or vomiting, marked prostration (indicated by a small, rapid, and irregular pulse), pallor (sometimes attaining lividity), cold sweats, rigidity of the abdominal wall, meteorism, anxiety, and fear of a fatal issue.

> A very rapid and considerable meteoric distention coming on after a contusion of the abdomen does not of itself, in the absence of characteristic signs and when the pulse is good, point to a rupture of any of the viscera, or to an internal hemorrhage. Lejars (Semaine médicale, Oct. 30, 1907).

All these symptoms bear the imprint of a severe nervous commotion, and, if the extensive distribution of the sympathetic nervous system in the abdominal cavity is borne in mind, the fact will become evident that symptoms usually witnessed immediately after the receipt of the injury are due mainly to the influence of the concussion upon the sympathetic supply. Sudden death has been known to follow a violent blow, especially when received in the region of the solar plexus.

> Any contusion of the abdomen may induce symptoms of shock. It is impossible to determine the extent of the internal injury from the presence or the intensity of the shock or the total absence of signs of shock. The writer has had patients with severe laceration of the liver or rupture of the bowel who were able to repair to the hospital on foot. Subnormal temperature may be due to the shock and anemia; fever soon after the trauma shows an inflammatory process. The pulse and heart action are not influenced by internal injury except in case of anemia or peritonitis. Nausea and vomiting do not necessarily accompany anatomic injury. Föderl (Med. Klinik, Oct. 30, 1910).

The pain varies according to the location of the traumatism and the sensitiveness of the patient. Very severe at first, it usually becomes less marked after a few hours. It is greatly influenced by shock, profound prostration reducing its intensity by reducing sensation. Great restlessness usually accompanies abdominal pain after injuries, as well as during other diseases, such as appendicitis, when the suffering is due to a localized trouble. The pain may be radiated in various directions,—the shoulder, the umbilicus, the left axilla, the testicles, etc.,—according to the site of the primary lesion. Local tenderness is usually marked over the site of the traumatism.

> Rigidity of the abdominal muscles, attended with dullness, even slight in degree, and local tenderness, are most valuable points in the diagnosis of these injuries, and where they exist, and especially if a blood-count shows an active leucocytosis, operation is demanded and no time should be lost in performing it. It is very hard to convince the patient and his friends of the actual condition, and they will invariably plead for delay. The serious condition should be early pointed out, and every effort made to secure consent to operate while the condition of the patient renders success probable.
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> These cases are most inevitably fatal without operation, and the effect of an exploratory incision while the patient is in a fair condition is not serious enough to counterbalance the advantages to be gained if rupture of any of the organs is found to exist. W. G. Weaver (Penna. Med. Jour., July, 1904).
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> Protest against the administration of opium or other narcotics until the diagnosis is positive, because they obscure the clinical picture, the diagnosis, and

the indications for treatment. They should be reserved for use in cases in which the diagnosis is positive, or in which both removal and operation are impossible on account of surrounding conditions, or in those cases in which the injury is so serious that death is inevitable. Föderl (Med. Klinik, Oct. 30, 1910).

The vomiting varies greatly in intensity from mere nausea to the most violent expulsive efforts, which are liable, by the strain upon the abdominal organs, to suddenly increase the extent of the lesions. The vomited matter sometimes contains blood, especially if the upper portion of the digestive tract is involved in the injury. Constant and persistent vomiting tends to indicate a contusion accompanied by visceral lesions. According to Berndt, in simple cases the vomiting is repeated but two or three times. When the intestine is ruptured the vomiting is persistent and intractable and liver-dullness is absent.

The degree of shock depends upon the nature and extent of the injury and especially upon the amount of blood lost. When the signs of collapse gradually become more marked, internal hemorrhage from rupture of one or more of the viscera is to be feared.

The pulse, usually rapid and weak at first, gradually becomes stronger and slower if a favorable reaction is about to take place. If, on the contrary, an unfavorable course is being taken and some complication is to occur, its rapidity and tension may become increased. Irregularity is not a favorable indication if it persists. Temperature is independent of the pulse, except when a favorable reaction is taking place, when it may return to the normal line after having gone beyond or below it. The usual belief that a subnormal temperature always follows internal hemorrhage is fallacious; for it may also be raised. The temperature, therefore, is of no value as a guide.

Hematemesis may assist in establishing the diagnosis of lesion in the stomach or the upper portion of the intestinal tract, while the presence of blood in the stools may do the same as regards lesions of the intestines as a whole, including the colon. But, in itself, this symptom is, by no means, characteristic, since a violent strain may cause sudden engorgement of pharyngeal, gastric, rectal, or hemorrhoidal vessels and then, several days after the accident, blood-rupture ensue. Even when present, streaks in vomited matter or stools are not always indicative of an alarming condition.

Blood in the urine is a more reliable sign of lesion in the urinary tract, especially the kidney and bladder. Anuria is also indicative of lesions in these organs; but, as shock frequently arrests the flow of urine, it is only valuable as a symptom after all symptoms of shock have passed.

Hemorrhage into the orbits and from the ears are occasionally met with when the concussion has been very severe. This symptom does not necessarily indicate that the injury is an unusually dangerous one.

A few hours after the accident the pain usually becomes reduced; the patient may be more quiet and, perhaps, somnolent, although the pulse remains in its former condition. This period lasts between twelve and twenty-four hours. If at the end of this time there be no complication,

a visceral lesion is probably not present. If, on the contrary, the symptoms gradually increase in intensity, the likelihood of grave injury is very great.

In the light of present knowledge, however, the practitioner should not delay active procedures until the patient's life becomes compromised by permitting the mechanical injury produced to start an infectious process, when the manner in which the injury was inflicted and the force applied tend to suggest serious internal lesion. An exploratory incision is sometimes permissible (see colored plate).

> A measure almost devoid of danger is the simple, exploratory abdominal incision, to determine whether or no a visceral lesion exists. It is a well-demonstrated fact that any fluid or extravasated matter in the peritoneal cavity will almost invariably present itself under the line of incision where the cavity has been entered, being forced there by the intra-abdominal pressure, and it is on this principle that abdominal drainage can be effected against gravity. The writer has seen a large collection of pus in the pelvic cavity drained through an opening in the belly so completely that at the autopsy not a spoonful remained. It follows, then, that in many cases at least a simple incision through the abdominal wall will be all that is necessary to reveal even a small extravasation through a ruptured viscus. Of course, there will be cases in which the rupture is so minute as to preclude extravasation at the onset, and such will be overlooked. In doing this little operation, for, as a rule, a short incision will be as effectual as a longer one, it is absolutely necessary that all bleeding be checked before opening the peritoneum, lest some of the blood should find its way into the cavity and obscure the findings. When and where shall the exploratory incision be made? At the earliest possible moment, for in this lies the salvation of the patient, and in the absence of contraindications it should be made in the median line between the umbilicus and pubes. D. Tod Gilliam (Monthly Cyclo. of Pract. Med., May, 1907).

Two classes of cases should not be operated on at first: (1) Cases in which little or no shock is present, and in which there are absolutely no localizing signs; (2) cases in which profound shock, amounting perhaps to collapse, exists. Immediate operation is demanded in persistent moderate shock, with or without localizing signs. Immediate operation is indicated in cases of progressing hemorrhage, and in cases of peritoneal infection. Scudder (Boston Med. and Surg. Jour., May 2, 1901).

Any injury to the abdomen, though no external injury occur, may be associated with damage to the intestine or other viscera. An exploratory operation is justifiable in cases with distinct rigidity. An operation is absolutely indicated when there is, besides rigidity, pain, tenderness, vomiting, shock, dullness, or other symptoms indicative of some intra-abdominal disturbance. Cases not operated upon are lost. The importance of early operation cannot be emphasized too strongly. At present the death-rate is about 75 to 80 per cent. Flint (Med. Record, Feb. 18, 1905).

Series of 64 cases in which the duodenum was the seat of the lesion. An operation was done in 28 cases, but in 6 the perforation was not discovered, and in 7 the patients succumbed to shock, hemorrhage or complications. Injury of the duodenum may be followed by thrombosis of the portal vein. Notwithstanding the bad prognosis, treatment can be by operative measures only. Small holes in the duodenum may be sutured, but extensive injury requires resection of the intestine. It is not particularly difficult and proved successful in the case reported, as also in others on record. Transient glycosuria was observed in this case and also in several in the literature. Meerwein (Beiträge z. klin. Chir., liii, Nu. 3, 1907).

Cases illustrating the fact that the advantages of an early operation are too

great to warrant waiting until alarming symptoms develop before operating. The diagnosis is not only difficult at first, but frequently impossible, especially when there is shock. It is better to operate prudently in a doubtful case than to run the risk of compromising the chances of success should operation be necessary. Patry (Revue méd. de la Suisse Romande, Feb. 20, 1909).

DIAGNOSIS.—In abdominal contusions the diagnosis should primarily be based upon the history of the accident, the manner in which the injury occurred, the shape of the body, or bodies, by means of which the traumatism was inflicted, and the degree of percussive force applied, and, secondarily, upon the symptoms present.

The diagnosis of traumatic lesions of the abdomen is most difficult, the symptoms being variable. When there is an element of doubt in diagnosis, laparotomy is indicated. History and nature of injury may be the only indications, but early laparotomy will improve the percentage of recoveries. Laparotomy as a means of diagnosis is without danger. Sellenings (N. Y. Med. Jour., Jan. 19, 1907).

Method of abdominal diagnosis which, although purely clinical, is known and largely used abroad, but in spite of its great usefulness is seldom heard of here. This is the practice of making abdominal or bimanual vaginal examination of patients while in a hot bath. Unless one has tried this procedure, it is difficult to conceive of its immense usefulness, for in many, if not most, instances the abdominal relaxation obtained is quite equal to that obtained under an anesthetic, with the added advantage that the patient can help the examiner by voluntary movements, such as deep inspiration, holding the breath, etc. This can be done in an ordinary bathtub, in water as hot as the patient can bear; or if it is desirable to have the patient higher in the tub, a long sheet may be let down over the tub into the water and fastened about the ends of the tub by knotting the corners under the rolling edge. Carter (Med. Record, May 7, 1910).

Lesions of the Intestinal Tract.—Various theories have been advanced as to the manner in which rupture of the intestine is brought about, but experiments have shown that squeezing of the gut between the compressed abdominal wall and the vertebral column is the main mechanical factor brought into action.

Five cases of subcutaneous rupture of the intestines, with three recoveries. All the patients in this series were injured in one or two ways. Either the patient fell heavily, striking the front wall of his abdomen on some hard angular body, or else a heavy body fell on him while supine. The writer believes that in this way the bowel is cut in two by the angle or promontory of the sacrum, against which it is forced when the anterior abdominal wall is pushed against the spine. Andrews (Surg., Gynec. and Obstet., June, 1906).

Crushing against the ilium is rarely produced. Another, although rare, cause of rupture is the presence, in the intestinal tract, of liquid or semiliquid material, the sudden circumscribed pressure exerted upon the gut causing it to burst, through overdistention. The small intestine is the seat of lesion in 75 per cent. of the cases of rupture in the course of the intestinal canal. Hence the importance of carefully ascertaining in each case the direction from which the percussive force came, the intensity of that force, and the relative position of the organs between the site of pressure and the spinal column.

Another factor of importance in establishing a diagnosis is the size of the instrument causing the injury.

Lesions of the digestive canal, for instance, are usually the result of violent and sudden percussion produced by a body over a limited surface of the abdominal wall.

The predisposing factors are the presence of solid, semisolid, or fluid matter in the hollow viscera; leanness of the individual, and intestinal adhesions.

Any of the above accidental causes of injury being fulfilled, rupture of some portion of the gastrointestinal tract is likely, especially if there is loss of consciousness at the time of the accident, followed by collapse, severe pain, a rapid and weak pulse, vomiting, tympanites due to the escape of intestinal gas into the abdominal cavity, and tenderness and rigidity of the abdominal walls.

Summary of 64 cases found in the literature of injuries of the duodenum from contusions, besides one of his own. Among the symptoms noted were bilious vomiting soon after the accident, rigid abdominal walls, absence of an area of dullness over the liver, localized pain and shock. Fränkel lays great stress on the slow rise of the temperature from hour to hour. Pulse above 100, if hemorrhage can be excluded, speaks in favor of rupture of the intestines and incipient peritonitis. Circumscribed pain and tenderness are indications for exploratory laparotomy. Meerwein (Beiträge z. klin. Chir., liii, Nu. 3, 1907).

The wound of entrance made by modern projectiles may be smaller than the diameter of the bullet. The firing distance is of great importance. At a distance less than 300 meters the explosive manifestations are very marked; in distances over 300 meters pure perforations are produced. The power of penetration may have been lessened, so that the projectile may lodge in any organ of the body; secondary infection of other organs may follow. The frequent shooting in the reclining position leads to very complex injuries. The bullet may enter the apex of the lung and have its exit in the floor of the pelvis. The caliber of the wound is narrow in the glandular organs of the abdomen. The entrance and exit wound may be of the same size; in exceptional cases only is the wound of exit lacerated. In grazing shots the borders of the wound are sharp and well defined. The caliber of the wound is more circumscribed in the pancreas and kidney than in the spleen or liver. The abdominal organs may be crushed by shots at close quarters. Von Doche (Militaerarzt, July, 1909).

Such a diagnosis is further strengthened by hematemesis or bloody stools, the former tending to indicate a lesion of the stomach. Death occurs in 96 per cent. of such cases if unoperated.

There are two chief mechanisms by which lesions of the intestine by abdominal contusions are produced: (1) *Crushing* of the bowel against the vertebral column, and (2) *bursting* of a loop of gut. The former is the more common, the dangerous blows being directed anteroposteriorly if applied in the median line, or obliquely inward if applied laterally, in either case pressing the bowel forcibly against the spine. Much less dangerous are blows directed obliquely outward if applied to the median line, or those directed almost parallel to the anterior abdominal wall. The smaller the striking surface of the agent the greater the risk of intestinal lesion, the parenchymatous organs being especially involved when the striking surface is large. The mucous membrane gives way first, then the muscular, and lastly the serous coat, so that the resulting wound is funnel-shaped with the base directed internally. For a lesion to be produced by *bursting*, the communication of the intestinal loop with the loops above and below must be momentarily intercepted by the injuring force, the loop must be distended with fluid or gas, and the striking surface is usually large. The serous coat gives

way first, and the wound is funnel-shaped with the base external. The rupture usually occurs at the summit of the loop. C. Dambrin (Revue de chirurgie, vol. xxix, No. 3, p. 457, 1904).

Case of traumatic rupture of the intestine by indirect violence in a woman of 26 whose previous health had been good. While hurrying into her house to escape a thunder-storm she slipped and fell, striking the ground upon the right buttock. She had just partaken of a hearty supper. No immediate alarming symptoms were noticed. She was awakened in the middle of the night by severe abdominal pains. The abdominal symptoms rapidly increased, and two days after the fall the patient was in a critical condition. The temperature was 104.3°, the pulse 140. There was marked tympany.

Case in which, on opening the abdomen, there escaped cloudy fluid, but no gas. On separating the adhesions which had formed about the great omentum there was a gush of fluid heavily loaded with fibrinous flakes. The small intestine was distended and of a bluish-black color. A small perforation was discovered on the convex surface of the lower portion of the jejunum. This was sutured into the abdominal wound. The abdomen was drained. The shock of the operation was considerable, but on the second day there was improvement. The fistula persisted. Three months later, the fistula continuing to discharge, the patient had become alarmingly weak owing to the failure in assimilation of food, all effort to heal the fistula having failed. A second operation was done, the fistula was closed, and the continuity of the gut restored. Recovery was rapid, and in the next few months she gained 25 pounds in weight. E. J. Senn (Amer. Jour. Med. Sciences, June, 1904).

The effects of contusions of the abdomen upon the intestinal ligaments, upon the mesocolon and the mesentery, have not been much studied. The intestinal arteries that are injured in lacerations of the mesentery are the superior and inferior mesenteric arteries or their branches. A wound of the secondary branch of the superior mesentery far from the intestine does not, owing to the richness of the anastomosis, cause gangrene of the intestine; but, if the branches are cut or injured near the intestines, gangrene will follow. Here are some of the results of the experiments: Section of the superior mesenteric artery; gangrene of a long portion of the small intestine; section 8 centimeters in length, along the border of the mesentery in such a way that all the recti vessels are divided close to the intestine; gangrene of the intestine for 4 centimeters; incision of the mesentery, 5 centimeters from the mesenteric border of the intestine; placque of superficial gangrene of the intestine; incision 8 centimeters from the mesenteric border of the intestine; intestine is not involved. The closer these lesions are to the intestine, the more serious are their consequences.

These anatomical and physiological notions have their importance in therapeutics; in fact, early death from hemorrhage is inevitable if one does not intervene surgically. If, perchance, patient should survive this hemorrhage, he soon would be exposed to gangrene of the intestine and to peritonitis. Hence, early laparotomy is indicated in these cases. Every time the tear is located near the intestine an enterectomy of the corresponding intestinal zone is indicated. If it is parallel to the axis of the mesentery and at some distance from the mesenteric border of the gut, simple ligation of the vessel will suffice. Further, one can fix an omental graft upon the intestine so as to assure collateral circulation. A. Labastie (Arch. gén. de chir., Jan. 25, 1908).

Study based on 2500 cases recorded in various hospitals. It has been recommended that the abdomen should be explored in all cases of severe abdominal injury, and that the question of diagnosis may be left until the parts have been actually exposed by operation. There can be no doubt that the exact lesion or lesions may sometimes be difficult or even impossible to define, but an attempt should faithfully be made to come to a conclusion before the

abdomen is opened; an operation should not be done "on the chance," but all the symptoms carefully noted and weighed after a systematic examination of the patient.

If it is possible to ascertain the exact part of the body struck by the force which caused the injury, then one can make an approximate guess as to the organ ruptured, for it is generally lying beneath, between that point and the spine, and incision over this area gives direct access to the damaged structure. W. H. Battle (Practitioner, July, 1910).

In the differential diagnosis of abdominal contusion the greatest feature for an early recognition of the existing conditions is whether there is unilateral or general tension of the abdominal wall, unless there is considerable blood-suffusion at the injured place. Aside from the reflex tension of the abdominal muscles, a slight, but distinct exacerbation of the general condition during the first few hours following the injury is a point of importance. With very careful observation, three or four hours may be allowed to elapse, but even then there is the possibility of error. Koerte reported a case where he was absolutely certain of his diagnosis and had decided to operate; the patient, however, refused operation and made a smooth recovery.

In the *most favorable cases,* where is but a slight tear, the mucous membrane will prolapse and occlude the aperture. Neighboring loops or the omentum will form a layer over the lesion with agglutination or adhesion, so that recovery may take place. If there is exudation of intestinal contents, a circumscribed, encysted abscess may form which is capable of resorption, or secondary perforation into the intestine or outward may occur; but it is equally possible that pus will find the dangerous route into the free abdominal cavity.

In the *most unfavorable cases* there is neither occlusion nor abscess formation; the inflammation will rapidly spread over large areas or over the entire peritoneum and cannot be checked. As early as four hours, exudate may be found; likewise, fibrinous deposits on the various loops. The more or less fulminating course is not only dependent upon the quantity of the exudate, but also on its infectious nature. This differs in the various sections of the gastrointestinal tract, as has been shown by Brunner, and, according to him, the greatest weight attaches to physical factors (variations in consistency) favoring the propagation of infectious material. For this reason he considers lacerations of the small intestine more dangerous than those of the large intestine, as in the former the quantity of bacteria increases toward the cecum.

Statistics show the rarity of cases in which the most favorable course, as depicted above, takes place. Of 160 cases of subcutaneous intestinal rupture in which the expectant treatment was instituted, 149 died; of the 11 which recovered, 10 had to be operated during treatment for fecal abscesses and fistulæ. These figures furnish, in the writer's opinion, clear and distinct proof for the insufficiency of expectant treatment, which, indeed, should be totally discarded. Enderlen (Post-Graduate, July, 1911).

Lesions of the Stomach.—Blows seldom cause rupture of the stomach, the elasticity of the organ, even when containing liquid or semiliquid material, being such as to cause it to escape injury under sudden impact or great pressure. It is also protected by the lower ribs, the liver, and the intestines. Nevertheless, this organ is occasionally involved in traumatism affecting other abdominal viscera. In the majority of cases the rent is found near the pyloric orifice, but the greater curvature may be the seat of the lesion, while the entire organ is occasionally torn from end to end. In the latter case, however, death ensues almost immediately in practically all cases. Pressure during lavage of the stomach

may also cause laceration of the mucous membrane.

In the case of incomplete tears there may be hematemesis and severe localized pain resembling that of gastric ulcer,—gnawing and burning in character. This is followed by localized inflammation with tendency to the formation of adhesions. Hemorrhage between the coats of the stomach may also occur in incomplete tears, a cyst-like pocket being formed.

Violent pressure upon the stomach may cause it to be crushed against the spinal column, and the mucous surfaces be lacerated by interpressure of the anterior and posterior walls of the organ. In such a case a marked lesion necessarily follows, giving rise to copious hematemesis.

Rupture of the stomach implicates the peritoneal coat in the majority of cases, the elasticity of the peritoneal investment being less than that of the two internal coats: muscular and mucous. The contents of the stomach, or a portion of them, escape into the peritoneal cavity and cause severe suffering and shock, followed promptly by death or septic peritonitis. Bryant teaches that a ruptured intestine is probably present, though this is not certain, when, after a diffuse injury to the abdomen or a severe local injury as the immediate result of the accident, there is little collapse, and when vomiting soon becomes a prominent and persistent symptom, with lasting local pain and great thirst, with or without abdominal enlargement.

According to Gluzinski, two signs which enable the physician to diagnose the occurrence of intestinal perforation before peritonitis has had time to manifest itself: 1, distinctness of the murmurs of the heart and respiration during auscultation of the abdomen, due to the presence of intestinal gases in the peritoneal cavity. 2, change in the pulse, which, at the moment of perforation, becomes accelerated, to slacken some hours later, owing to the absorption of putrid gases acting as cardiac poison.

> Four symptoms of internal abdominal injury are especially important and trustworthy: 1. Permanent and progressive feebleness and frequency of the pulse, especially if combined with pallor, a general state of anxiety, of depression, or of delirious excitement. Abdominal tenderness soon after injury or after the onset of acute symptoms may indicate hemorrhage rather than inflammation. 2. Loss of liver dullness with progressive gaseous distention of the abdomen, or tenderness and resistance of the parietes. This indicates perforation of the gastrointestinal tract. 3. Limited dullness on percussion without distention is also produced in some cases of perforation. 4. Shifting dullness in one or both flanks as is observed in cases of ruptured bladder or large hemorrhage. C. A. Ballance (Lancet, Oct. 29, 1904).
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> Case in which laparotomy, after a severe contusion of the abdomen, revealed an extensive tear of the mesentery as the only resultant injury. Gangrene of the ileum had commenced as a result of the laceration of the nutrient vessels. Reinecke (Münch. med. Woch., Sept. 8, 1908).

Lesions of the Liver.—The liver, owing to its friable nature, its size, and its anatomical position, is the organ most frequently injured, because indirect concussion may cause a profound lesion. A fall from a great height into water may thus cause a gaping rent of the capsule and parenchyma and open a large number of vessels. Severe and sudden blows of any kind, especially

those involving much surface, over the abdominal wall may thus cause injury to this organ. Again, its softness, which may be increased by hypertrophy, cause it to yield readily to the crushing produced by carriage-wheels, car-bumpers, etc.

The severity of all the general symptoms is usually increased. The pain, when the liver is seriously injured, is peculiar; it radiates from the right hypochondrium to the waist, the scrobiculus cordis, or the scapular region. The respiration is generally embarrassed; there is marked shock. Examination of the feces may show the absence of bile, especially if the bile-duct is ruptured: an occasional complication. The dissemination of bile in the system causes itching and, after a time, jaundice. The escape of bile into the peritoneal cavity may not give rise to peritonitis, however, this fluid being aseptic. A serous exudate may result from the irritation caused by its presence, forming a composite fluid which may be retained in the peritoneal cavity a considerable time.

> Rupture of the liver is an extremely fatal accident, and the symptoms which ensue are usually marked and serious. Shock is present, frequently passing into collapse and death. Short of this there are vomiting, rapid pulse and respiration, pallor, etc. In this accident rigidity of the abdominal wall is very evident, so that it may appear board-like. Tenderness becomes localized to the hepatic region, and there is shifting dullness in the flanks with the ordinary symptoms of loss of blood, according to the amount of it which is effused; the man becoming restless with a rapid, weak pulse, sighing respiration, and what is called "air hunger." Jaundice may be a late symptom and is therefore of no use in the early diagnosis, which is so very important.
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> There is, as might be expected, much variation in the size of the rupture, which is usually on the convex surface of the right lobe; the combined statistics of Mayer and Ogston give 3 right lobe to 1 left lobe as the proportions.
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> Shock in this injury may not be evident when the patient first comes under observation. When leaving the Royal Free Hospital some years ago the writer saw a woman of 59 brought in, who had been run over in the street a few minutes earlier. She was excited, and resented examination. There were no marks on the abdomen, no dullness in the flanks, or rigidity of the muscles. It was difficult to induce her to remain in the hospital, yet three hours later the abdomen was full of blood, and she did not survive operation to arrest the bleeding for very long. The liver was extensively torn, and the kidney showed a recent laceration; there were other injuries also. W. H. Battle (Practitioner, July, 1910).
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> The most reliable symptom is the *défense musculaire* emphasized by Hartmann and Trendelenburg. Rigidity is not the proper term for this condition, for rigidity rather denotes a tetanic state of the abdominal muscles, whether stimulated by pressure of the hand or not. It is not marked, except in the gravest cases, shortly after injury, but develops in the following few hours from irritation of the peritoneum by the hemorrhage of intestinal contents from rupture of the intestines. It was especially mentioned twenty-four times in the 44 cases, and in the remainder other signs, notably those of internal hemorrhage, were so marked that it was not noted in the history. Nevertheless, it is not an infallible symptom, as proved by 2 cases related by Baum. Riebel (Quarterly Bull. N. W. Univ. Med. School, Sept., 1910).

A rent is probable after a severe injury if there is collapse, if the pulse becomes more rapid and small, if the patient shows signs of exsanguinity, if the area of liver-dullness on percussion is increased, and if pain

radiating to the scapular region is complained of. Severe injury may exist, however, without these indications.

The liver is injured with greater frequency than any other abdominal viscus. Of 365 cases of subcutaneous injuries of solid viscera the liver was injured in 189. The spleen, kidney, and pancreas combined in but 179. The factors which favor a high percentage of injury are: (1) It lies wedged between the ribs and vertebral column, and (2) it is very heavy and elastic and only slightly movable. It is nine times as heavy as the spleen and ten times as heavy as the kidney. Furthermore, the physiological function of digestion renders it more liable to injury, since the gland is engorged with blood. Again the organ is particularly liable to disease. Alcoholism, tuberculosis, malarial lesions, new growths and the production of fibrous tissue rendering it even more friable than in its normal condition. B. T. Tilton (Annals of Surg., Jan., 1905).

Case in which a man, 19 years old, suffered from a contusion, with possible rupture of the liver. Four days later jaundice appeared on the scleræ and biliary coloring matters in the urine. The jaundice spread thence over the entire skin of the body, the urine became dark brown, and from the seventh day on the patient suffered from extremely severe attacks of colic. At the beginning of the third week the area of liver dullness was markedly small. The attacks of colic were ascribed to adhesions, and finally laparotomy was performed with a view to their relief. About 4 liters of bile-stained ascitic fluid escaped when the peritoneal cavity was opened, numerous adhesions were broken up, and a fibrinous exudate was wiped away from the surface of the intestines. Palpation of the liver revealed that that organ was very atrophic, but no operative measures were directed to its relief, and the wound was closed. At first little change was produced in the condition of the patient. Ten days after the operation an abscess was opened in the cicatrix, and then he began to improve. The area of liver dullness gradually increased until it finally reached the border of the ribs in the right mammillary area, but its lower margin could not be felt on palpation. The general health of the patient had also become very good. Mekus (Münch. med. Woch., Jan. 8, 1907).

History of 8 cases of injury of the liver in which an operation was performed in less than four hours in all but one, in which the interval was ten hours. They emphasized the advantage of suturing the wound in the liver whenever it is at all possible. The writer sutures through a tampon to prevent bleeding later. He has recently examined 3 of the patients after an interval of from several months to two and a quarter years, and found them entirely well and free from disturbances of any kind. Noetzel (Beiträge z. klin. Chir., xlviii, Nu. 2, 1906).

Case of subcutaneous injury to the right lobe of the liver. The patient had fallen from his horse and his abdomen had borne the weight of the horse and of the saddle. Diagnosis of internal hemorrhage was made. After a minute exploration of the abdominal cavity, a bleeding wound of the right lobe of the liver was seen. The hemorrhage was stopped by tamponade; the patient recovered. The diagnosis is to be made only after the abdominal wall has been opened, and then it is made by seeing the seat of hemorrhage.

We are still in doubt as to which way is better, to suture these wounds of the liver, or to pack them. The author prefers packing. He thinks it is more rapid, less difficult, and more reliable. The liver must be compressed from below up toward the diaphragm. Only iodoform gauze should be used. Von Kippel (Arch. gén. de chir., Dec., 1907).

Seven cases of injury of the liver in which surgical treatment was successful in 3. The injuries in the cases with a favorable outcome were: A bullet wound, a kick from a horse, and injury from being run over. The others were

very serious contusions with other injuries. Rigidity extended over the entire abdomen in every case, and the pain on palpation was also diffuse, although more pronounced on the right side. Tamponing alone arrested the hemorrhage in the three favorable cases. The pulse gave no signs of the internal bleeding, being relatively good even in the most rapidly fatal cases. In one instance the gauze tampon answered a double purpose, draining a pus pocket that developed between the diaphragm and the liver. The writer's experience confirms the value of tamponing as the best, safest, most rapid and effectual method of arresting hemorrhage in case of rupture of the liver, although a suture may be advisable for a smooth and conveniently located stab wound. Dencks (Deut. Zeit. f. Chir., lxxxii, Nu. 4-6, 1907).

In the diagnosis of injury of the liver bradycardia is a suggestive sign. In one case the liver had been ruptured by the kick of a horse and the pulse was only 48. In the other case the liver had been sutured and the pulse was 52. Several writers have mentioned bradycardia with injury of the liver, and ascribe diagnostic importance to it. The writer experimented on animals to determine the influence on the pulse of injury of liver and spleen. The results with 20 animals showed that bradycardia is a characteristic symptom of injury of the liver, but that its absence does not exclude injury of this organ. Finsterer (Archiv f. klin. Chir., Bd. xcv, Nu. 2, 1911).

In 8 cases of rupture of the liver operated in the last five years, the writer noted that in 2 of the cases the fundus of the eye showed changes recalling those of albuminuric retinitis. These patients were men of 18 and 30 with severe contusion of the liver region and rupture of the liver requiring suture. In 1 case the changes in the fundus had subsided by the end of the second day. Tietze (Archiv f. klin. Chir., Bd. xcv, Nu. 2, 1911).

Lesions of the Gall-bladder or Biliary Ducts.—Blows and other conditions capable of causing hepatic rents sometimes implicate these organs in the lesion. There may be severe pain in the right hypochondrium if a rupture exists, vomiting of food and bile, and icterus. The urine is usually dark-mahogany and the stools ash-gray in color. Tenderness over the hepatic region is usually marked. The intensity of the symptoms depend to a degree upon the quantity of bile voided into the abdominal cavity; but, this secretion being aseptic, peritonitis only occurs as a complication when the peritoneum is itself implicated in the traumatism, or when the lesion is at the junction of the biliary tract and the intestinal canal, the latter in that case acting as a source of infection.

Escape of venous blood with or without bile, particularly in stab wounds over the region of the liver, is a very important sign. Hepatic injuries usually cause pain to radiate to the right shoulder. Inasmuch as there is also local pain on respiration, the chest does move as much on the right as on the left. This may lead to a misconstruction of the diagnosis, for it suggests to the casual observer thoracic injury. The blood gravitates into the right iliac fossa and may give well-marked dullness. Disappearance of liver dullness is due to beginning tympanites and is therefore not of great diagnostic importance. Jaundice is occasionally present, but usually does not appear until the second or fourth day. Ludwig found it 24 times in 267 cases. Its presence usually signifies injuries of the bile-duct. B. T. Tilton (Annals of Surg., Jan., 1905).

Lesions of the Spleen.—The causes of injury to this organ are the same as those of the liver. Rents, sanguineous infiltration, and partial crushing are the lesions most frequently observed. Enlargement of spleen through a malarial cachexia

renders it susceptible to lesions which traumatism would not give rise to were it in its normal state.

In extensive lesions copious hemorrhage usually takes place and death rapidly follows. If the lesion present is less severe, however, and the hemorrhage be moderate, there is tendency to collapse, increasing pallor, and a feeling of suffocation. The latter symptom and severe radiating pain in the region of the spleen are generally present, besides the signs peculiar to all abdominal injuries. If the patient survives sufficiently long the immediate effects of the traumatism, peritonitis or abscess and other complications frequently result. Severe local pain generally continues for some time, and chills are not infrequent. Percussion shows the organ to be more or less enlarged.

According to Trendelenburg, vomiting is a most important guide in the diagnosis of rupture of the spleen; in simple contusion of the alimentary tract it seldom if ever occurs.

History of 6 patients whose spleens were removed on account of the injury of the organ. There was no symptom specially characteristic of such injury, though signs of irritation of the peritoneum from effusion of blood demanded prompt intervention. Severe pain at the point of injury invariably accompanied serious damage within, however. In one of the cases the early intraperitoneal hemorrhage stopped spontaneously, but commenced again the third day, requiring operative measures. Noetzel (Beiträge z. klin. Chir., xlviii, Nu. 2, 1906).

Case of a girl of 4 who had been run over by a cab. The symptoms of shock subsided, the pulse became slower and fuller, and not until after seven hours were signs of internal hemorrhage observed. The abdominal walls did not become rigid until ten hours after the accident; the child had vomited blood twice during the interim. The abdomen was opened at about the twentieth hour and the ruptured spleen removed with the apparent complete recovery. The lower pole of the organ had been partly torn off. In a case in which the symptoms indicated rupture of the spleen the exploratory laparotomy revealed merely a few small subserous hemorrhages, and the abdomen was sutured without further intervention, followed by the complete recovery. Georgi (Münch. med. Woch., liii, Nu. 15, 1906).

A healthy spleen is seldom injured; the organ is usually already enlarged by some pathologic process or infection. Slight injury may cause only an absorbable hematoma, or, if infected, an abscess and adhesions which may discharge through adjacent hollow organs. Such outcome, however, is rare; the tear is usually through the envelope and rapid hemorrhage, calling for quick surgical intervention, occurs. E. J. Senn (Jour. Amer. Med. Assoc., Mar. 23, 1907).

Case of rupture of the spleen. The patient had received a violent traumatism in the left hypochondriac region, and had a few fainting spells. There was abdominal distention and tenderness. An exploratory laparotomy having shown serious intra-abdominal hemorrhage, the spleen was found torn and was extirpated. Raoul Baudet (Médecin Praticien, 1907; Surg., Gynec. and Obstet., July, 1908).

The symptoms of traumatic rupture of the spleen are essentially those of internal hemorrhage, and the diagnosis is usually not made until after abdominal section. The symptoms are obscure so far as enabling the distinction whether the spleen or some other abdominal viscera is ruptured. However, there should be no difficulty in diagnosticating the existence of hemorrhage into the abdominal cavity, and, when this condition is recognized, abdominal section is indicated. The incision should be made over the region of greatest dullness, if this can be determined. If percussion elicits a note

of higher pitch in one flank than in the other, a valuable hint as to the source of hemorrhage has been obtained. Should the hemorrhage be sufficiently severe to give a percussion note of equal dullness in all regions the indication is to make the incision in the middle line. The treatment is essentially surgical, the object being the control of hemorrhage, and all authorities are agreed that this end is most certainly accomplished by splenectomy. The mortality following removal of the healthy spleen for rupture is about 40 per cent., whereas that of non-operative treatment is probably 100 per cent. Watkins (Med. Rec., Mar. 14, 1908).

Lesions of the Kidneys. — The kidney is firmly held in place by its attachments, while its consistence is such as to preclude elasticity. Hence, a blow or undue pressure may cause rupture. All the causes of injury that may take part in the production of lesions elsewhere may also induce renal lesions, which may consist of contusion, rupture, or laceration.

Study of 5 personal cases and of 660 cases gathered from literature. The causes of rupture were varying, muscular action causing 10 per cent. The author was struck by the slight force necessary for rupture to take place. A blow over the front of the abdomen with the patient on his back was one of the causes of rupture. The kidney was never ruptured on one side with an accompanying injury to an organ on the opposite side. Intraperitoneal symptoms were usually due to rupture of the peritoneum. Tumor formation occurred in 143 cases. Hemorrhage was the frequent cause of death. In all the cases there was a striking absence of injury to the omentum or the intestine.

Indications for operation: (1) Marked and persistent hemorrhage; (2) presence of a rapidly increasing tumor or area of dullness in the loin; (3) development of a tumor in the loin ten days or more after injury; (4) immediate operation when there are signs of free fluid in the abdominal cavity; peritonitis or other peritoneal injuries. Watson (Trans. Amer. Assoc. of Genito-Urin. Surg.; Amer. Med., May 30, 1903).

The kidneys are not properly abdominal organs, being extraperitoneal, but their injuries are comparatively frequent, especially in young males, owing to their greater exposure. The mechanism is usually a bending or fracture of the lower ribs. One cause of the infrequency of the accident in women may be the mode of dress, the corset protecting the organ, though the greater thickness of tissues and the wider spread of the iliac crests are also suggested as factors by Kuster. E. J. Senn (Jour. Amer. Med. Assoc., Mar. 23, 1907).

Case in which the patient was kicked in the kidney region by a horse. The rupture occurred at the farthest point of the organ, the kidney having probably been dashed against the spine. Suarez (Annales d. Mal. d. Org. Gén.-Urin., xxiv, No. 17, 1907).

In the rapid recent increase in the number of reported cases, there is reason to believe that subparietal rupture of the kidney is more frequent than the literature would lead one to believe. Shock, injury to other organs, and external evidence of trauma are frequently absent. A history of an abdominal contusion, followed by rigidity and hematuria, is sufficient data to lead to an exposure of the organ. Slight lesions and complete rupture of the kidney cannot be differentiated by clinical signs or symptoms. Proof that there is an absence of serious rupture is called for before instituting the so-called expectant treatment. Nephrectomy should be reserved for very extensive disintegration of the organ. Conservative treatment, preferably by suture, is indicated in the majority of cases. Connell (Jour. Amer. Med. Assoc., March 25, 1911).

Besides the symptoms common to severe abdominal traumatism there may be increased pain in the lumbar region with radiations in the direction of the pubis and rigidity of the

muscles. Dullness on percussion is sometimes elicited. Anuria may also occur, but this is not a characteristic sign. Hematuria is an important indication of renal leceration, however, although it may not present itself at once; it may be followed by the appearance of pus. The catheter should be used in these. Retraction of the testicles is also said to occur (Rayer). The ureter is very rarely involved; when it is, the symptoms are not modified. Enlargement of the lumbar and hypochondriac regions is present in the majority of severe cases, but may supervene late in the history of the case.

Thanks to the compensatory work of the uninjured kidney, the mortality of renal lesions is not so marked as when other abdominal organs are injured.

Even severe wounds have been known to heal. If large renal vessels are torn, marked lividity occurs, the patient rapidly becoming exsanguine. Death may thus follow very soon. Involvement of the peritoneum in the injury is promptly followed by peritonitis, the signs of this affection appearing a few hours after the receipt of the injury. Sepsis is not an infrequent complication in unoperated cases.

Case of a boy, aged 16 years, who had fallen a distance of 2 meters during play, striking his back. Pain over the kidneys developed, but not sufficient to force him to stay in bed until the tenth day, when he began to vomit and develop an intense diarrhea. He bled from the nose and gums, and numerous petechiæ appeared over arms and legs. On the fifteenth day he voided bloody urine. The flanks were dull, the abdomen distended and tympanitic. Rectal examination showed a mass behind the bladder. Four weeks later a second purpuric eruption appeared all over the body. The urine was still bloody, and an ascitic accumulation was noted within the abdominal cavity. The red corpuscles were reduced to 3,200,000; there were 334,000 hemoblasts; the blood did not clot nearly as readily as normally, and numerous myelocytes were present. Complete recovery ultimately resulted. E. Lenoble (Arch. des mal. du cœur, i, 475, 1906).

Two cases in which both patients fell on the loin, the one falling on the edge of a stair, the other on the edge of a pail. In both cases blood was present in the urine immediately after the accident and the ruptured kidney could be felt by palpation. In both cases it extended round the abdomen toward the umbilicus and was tender to touch, the swelling being clearly behind the peritoneum. Andrew (Lancet, Jan. 26, 1907).

Case of a man who was under treatment for about three weeks with the clinical diagnosis of contusion of the right kidney, hemothorax on the left side, and possible injury to the pancreas. Autopsy showed that there had been a total rupture of the left lobe of the liver, which was in the process of spontaneous healing. Chiari (Berl. klin. Woch., Sept. 7, 1908).

In complete subparietal rupture of the kidney the patient will, as a rule, give a history of having received a severe blow in the side. The examination reveals a tumor in the loin. There is, as a rule, hematuria. The patient is in a state of profound shock. These symptoms, with evidences of internal hemorrhage, should lead one to treat the patient for rupture of the kidney. Prognosis depends upon the delay in applying the proper treatment. The primary mortality is due to hemorrhage, while secondary deaths are caused by infection, which may be hematogenous or ascending in origin. The mortality of all cases of subparietal ruptures of the kidney has been estimated at from 32 to 92 per cent. Bugbee (Med. Record, Nov. 5, 1910).

Owing to the rapid recent increase in the number of reported cases there is

reason to believe that subparietal rupture of the kidney is more frequent than the literature would lead one to believe. Shock, injury to other organs, and external evidence of trauma are frequently absent. A history of an abdominal contusion, followed by rigidity and hematuria, is sufficient data to lead to an exposure of the organ. Slight lesions and complete rupture of the kidney cannot be differentiated by clinical signs of symptoms. F. G. Connell (Jour. Amer. Med. Assoc., March 25, 1911).

The recent statistics of traumatic lesions of the kidney which showed a mortality of 14.6 per cent. in 143 cases with a conservative operation and of 16.7 per cent. in 131 nephrectomies, while 20.6 per cent. of the 427 patients not submitted to operative treatment died, are suggestive when we consider that only the severest cases are operated. The main points are to determine whether the vessels and the kidney pelvis are torn and whether there is infection. The intensity of the hematuria is not always an index of this. Cystoscopy, supplemented possibly by catheterization of the ureters, alone elucidates these conditions by showing whether the urine is being regularly expelled in a strong jet from the ureter mouth. If the urine is blood-stained, this shows which kidney is injured and that the pelvis and ureter are not torn, and that the passage from the pelvis to the bladder is open. If the bloody urine is expelled in approximately normal amounts and rhythm, conservative treatment is indicated, but, if no blood or urine enters the bladder from the injured kidney and none can be obtained through the introduced ureter catheter or there is merely blood or a few clots, there is evidently some laceration of the pelvis, permitting escape of the urine into the surrounding tissues, or the kidney has been destroyed to such an extent that the secretion of urine is arrested. In either case operative treatment is imperative. If stagnating urine is found in the pelvis, this excludes laceration. Operative measures should not be delayed. Stagnation of urine in the pelvis may cause intense pain, which evacuation of the urine relieves. Voelcker (Beiträge z. klin. Chir., Bd. lxxii, Nu. 3, 1911).

PROGNOSIS.—Death almost invariably attended rupture of the intestinal tract prior to the introduction of exploratory abdominal section, and prompt resort to active surgical procedures, when necessary, is indicated.

As to the liver, as late as 1864 wounds of this organ were considered as practically hopeless in every instance. While a very small proportion of these cases recover without surgical interference, as is shown by the scars occasionally found in the hepatic parenchyma, the fact remains that an exploratory laparotomy, permitting the surgeon quickly to arrest the loss of blood in case of hemorrhage and to rid the peritoneal cavity of accumulated extraneous fluids, has greatly reduced the mortality. The prognosis becomes much more unfavorable when peritonitis has set in, but a fatal issue may sometimes be averted, even in advanced cases of this complication, by surgical intervention.

Mayer in 1872 published statistics of 135 cases of subcutaneous traumatic rupture of the liver in conjunction with subcutaneous abdominal injuries. He gave a mortality of 86.7 per cent. Edler's compilation of 189 cases in 1887 showed a mortality of 85.7 per cent. for all cases and 78.2 per cent. for uncomplicated cases. One-third of all the cases died of hemorrhage. More recent collections of cases are as follows: Terrier and Auvray 5 deaths in 11 cases. Fränkel, 1901, 17 deaths in 31 cases. Wilms reported all cases occurring in the Leipzig Clinic during five years with 3 recoveries in 19 cases. Giordano's collection of 257 cases shows a mortality of 40 per cent. He con-

cludes that results have improved considerably since Edler's time. Riebel (Quarterly Bull. N. W. Univ. Med. School, Sept., 1910).

The same remarks apply to rupture of the gall-bladder.

Slight contusions of spleen heal readily, but rents and tears of any importance are frequently followed by fatal hemorrhage. Abscesses occasionally complicate convalescence.

The great majority of cases of rupture of the kidney that recover are those in which the initial lesion had been comparatively slight. In the graver cases, in which there is copious hemorrhage into the perinephric tissues or into the peritoneal cavity, of which the growing exsanguinity of the patient is an indication, the prognosis depends upon the speed with which adequate surgical procedures are instituted. Occasionally, however, the blood is held in check by the renal capsule.

Two cases in which a contusion reduced the secreting power of the kidney. In the first case the kidney was injured by a kick from a horse, and a latent nephritis developed with tendency to formation of stones; in the second case the blow left a cicatrix, palpable two years later, which interfered with the secretion of the organ, but did not seem to impair the general health. The prognosis in contusions of the kidney depends on the presence or absence of infection. The other kidney does not suffer unless the contusion is complicated by an infectious process. Simonin (Presse méd., Mar. 13, 1909).

The prognosis depends greatly, therefore, upon the patient's ability to stand operative procedures suitable to establish a positive diagnosis and bring the lesion that may at any moment destroy life within the immediate reach of art's highest powers. When serious injury is rendered probable by the nature of the accident, and the symptoms present also indicate a serious lesion, an exploratory incision, if the patient is not past relief, a careful examination of the organs involved, arrest of hemorrhage, closure of the disrupted tissues, or cleansing of the abdominal cavity may save him even when his condition appears almost hopeless.

Again, the prognosis is influenced by the time elapsing between the accident and the institution of surgical procedures. The sooner they are resorted to, all things considered, the greater the chances of success.

No case can be considered as hopeless unless a subnormal temperature, cold and cyanosed extremities, and other signs indicafe that the end is near.

Even when performed late in the history of the case, adequate operative measures sometimes prove successful.

The mortality in injuries of the kidney is, under the best surgical procedures, about 30 per cent. Death in these cases, if not immediate, as the result of shock, or hemorrhage, or injury to other important organs, is due (1) to anuria, (2) to infection, or (3) to secondary hemorrhage. Anuria is probably due to a reflex contraction of vessels in the sound kidney owing to stimulation of the splanchnics and the vagus endings (Masius). Secondary hemorrhage may not occur for a week or ten days after injury and is then due to a disintegration of blood-clots, which are acted upon by the urine. Infection may be (*a*) local, with deep cellulitis and subsequent general involvement; (*b*) peritonitis, or (*c*) an ascending involvement of the opposite kidney due to the breaking down of blood-clots in the bladder. Crawford (Amer. Jour. of Surg., Feb., 1908).

The early recognition of a rupture of the bladder greatly influences the prognosis. About 60 per cent. of the most unpromising lesion, intraperitoneal laceration, are saved by prompt surgical measures. The remaining 40 per cent. are unsuccessful mainly on account of delay in resorting to abdominal section. A favorable result has, nevertheless, followed laparotomy as much as fifty-four hours after the rupture.

TREATMENT. — Shock. — Shock or collapse, though unreliable as a sign of severe injury to the abdominal viscera, is, nevertheless, an alarming condition, especially if the temperature is subnormal and the breath is shallow, and it should at once receive attention. The patient is placed in bed with the **head low,** and a free supply of **pure air** insured, supplemented with **oxygen** if practicable. **Hot-water bottles** are placed around him and he is covered with blankets previously warmed, if possible, or wrung out of hot water.

Two main elements have to be borne in mind in this class of cases: (1) that the state of shock is due to a direct commotion of the sympathetic system with probable inhibition of the heart's action, and (2) the possibility of an internal lesion which may involve death by exsanguination or the outpour into the peritoneal cavity of gastric or intestinal fluids. While the first condition calls for stimulants adapted to sustain the flagging heart and restore the action of the vasomotor, the agents employed should not be administered by the mouth, since, in case of rupture of the stomach, the duodenum, or jejunum, a portion, at least, of the fluid may be added to those that may have found their way into the peritoneal cavity. **Rectal and subcutaneous injections** should be resorted to.

If no remedy be at hand, subcutaneous injections of 1 dram of **whisky** or **brandy** may be employed, and repeated every five or six minutes until reaction occurs. A **turpentine stupe** or a fresh **mustard poultice** (not plaster) over the xiphoid cartilage, and a **rectal injection** composed of a tablespoonful of turpentine, a raw egg, and a teacupful of warm water, sometimes act with surprising rapidity. Hypodermic injections of **ether,** or, better still, tincture of **digitalis** with $\frac{1}{120}$ grain of **atropine,** repeated in fifteen minutes, are necessary to sustain cardiac action. After the second dose the digitalis may be injected alone several times more. These measures are greatly assisted by **galvanic stimulation of the phrenic nerve,** the negative pole, moistened in a solution of chloride of ammonium, being applied to the neck in the depression immediately in front of the sternomastoid muscle, and the positive over the epigastrium.

These means are sometimes inefficient and **hypodermoclysis** should be performed. If a fatal issue seems inevitable, **saline transfusion** is indicated.

> In abdominal injuries due to blunt force the symptoms are referable to the abdominal wall and cavity, or both. Pain may be severe or slight. As an early symptom vomiting is constant, distention may be slow or rapid, rigidity develops later, shock may or may not be present. The temperature and pulse, particularly the latter, are considered of great importance. Opium, even in small doses, renders the diagnosis of such injuries difficult, and should never be administered early. After an abdominal injury, if there is tenderness,

acceleration of the pulse tending to increase ever so slightly, together with abdominal distention and a rise in temperature, the diagnosis of a grave injury is made absolute. In most cases but a few hours of close observation are required to establish the diagnosis. In such cases exploratory laparotomy should be performed at once unless the condition is so desperate that anesthesia means certain death. Fowler (N. Y. Med. Jour., Aug. 19, 1899).

In cases of abdominal contusion the surgeon before operating should wait for some symptom or symptoms indicative of intestinal injury. As in the presence of shock a diagnosis of intestinal injury cannot be made, the author would wait for reaction to take place. No one symptom is pathognomonic of intestinal injury, but the two most reliable are gradually increasing rigidity and an anxious, careworn, and painful expression of the face. The latter, which comes on after reaction has taken place and, it is supposed, is concomitant with development of peritonitis, is regarded as the most positive of all the symptoms of severe intra-abdominal injury. In the next group the author would place deep and perhaps radiating abdominal pain, respiration becoming more and more thoracic, vomiting after reaction, abdominal distention, increasing pulse-rate, and secondary fall in temperature. The subject of a severe abdominal contusion should, it is urged, be carefully and constantly watched. While advising delay in doubtful cases, the author does not mean that the surgeon should wait for serious symptoms to become so pronounced that a positive diagnosis is assured, for then operative intervention is, for the most part, too late. There is a positive midway between operating on every case and waiting for an assured diagnosis, where the surgeon can say that, owing to the gradual appearance of certain symptoms, there is fair reason to think that the intestinal tract may be injured, and that an immediate operation will give the best chance. Le Conte (Annals of Surg., April, 1903).

Immediate laparotomy is urged when the abdominal walls are rigid and there is local tenderness after a contusion, and when these symptoms display a tendency to increase rather than to subside. There is more shock when the injury is from an object acting on a large expanse of the abdomen rather than from the kick of a horse or the like. Normal temperature and full pulse do not exclude serious internal injury, and there was no vomiting in one of the most severe cases. Cautious percussion may reveal dullness corresponding to an effusion of blood, bile, stomach or intestine content or urine, and its progress can be thus traced in some cases. Schmidt (Deut. med. Woch., xxxii, Nu. 44, 1906).

Analysis of 17 cases of subcutaneous injury of the digestive tract in which an operation was resorted to, showing that operative treatment is imperative at the earliest possible moment when there is a probability that the stomach or intestines have been injured by a contusion. If the shock is too pronounced for immediate operation, every effort must be made to bring the patient out of the shock, with restoratives and saline infusion. In case of small circumscribed injuries, it may be sufficient to suture the wound in the intestine and to reinforce it with serosa drawn up over it, but in case of extensive injury it is better to resect the injured portion. Even if the patient is not seen until after the peritonitis is established, an operation is always justified, although the prospects of saving life are then small. Careful rinsing out of the entire abdominal cavity with large amounts of sterile salt solution should never be omitted, as this is the only means of cleansing the peritoneal cavity of infectious material. Voswinckel (Archiv f. klin. Med., lxxix, No. 2, 1906).

Treatment of contusion of the abdomen, based on 48 severe personal cases. In 31 cases the operation was performed early; 22 of these patients recovered, and 9 died; all the 6 patients with a tardy operation recovered also. Modern surgery can command incipient peri-

tonitis, but in the later stages it is difficult to handle. The vital energies can be sustained by administering **saline solutions** in extensive hemorrhage. If the vital energies have already ebbed too low, then the surgeon is powerless. In one of the writer's cases the intraperitoneal part of the full bladder had ruptured and a loop of small intestine had fallen into the organ. He sutured the bladder and transplanted the attachment of the peritoneum to the bladder, suturing it at a point lower down than normal, and thus making the seat of the wound extraperitoneal. There is no danger of peritonitis from rupture of the bladder if the rupture is entirely extraperitoneal. Hildebrand (Berl. klin. Woch., xliv, Nu. 1, 1907).

Immediate aseptic abdominal section is indicated in every doubtful case of abdominal injury. Important points in the surgical treatment of abdominal injuries: 1. Apply active measures to overcome or lessen shock, unless signs of active hemorrhage make quick action imperative. A reasonable time (one-half to three hours) may be allowed in cases of profound shock, to promote a helpful reaction. 2. Cleanse the skin as thoroughly and as widely as in any other abdominal case, notwithstanding the presence of indication for rapid work. 3. Precede an exploration by an intravenous **saline infusion** or a **transfusion of blood** when symptoms of hemorrhage are marked. As Crile has noted, "We may in this way transform a hopeless case into an average risk." 4. Make the search for intra-abdominal injuries thorough and systematic. 5. Cleanse the peritoneum thoroughly of septic material and blood, or fluid of any kind. This is best done by large gauze sponges, followed by copious irrigation, leaving the abdomen partly filled with saline solution. 6. Secure absolute hemostasis and water-tight repair of all wounds and ruptures. 7. Introduce drains whenever viscera have been penetrated or ruptured. 8. Use intravenous infusions of **normal saline solution** freely postoperatively in cases of marked shock or acute anemia. 9. Adopt the Fowler position and the live coil in all cases as soon as reaction from shock is obtained. 10. If intestinal paresis supervenes, **lavage** every four hours will accomplish more than enemata. Goodrich (Amer. Jour. of Surg., Jan., 1911).

Reaction.—As soon as reaction occurs in these cases another danger threatens the patient, that of hemorrhage, which the state of collapse has so far prevented to a degree, unless an extensive injury has caused overwhelming exsanguination. In this event, however, the patient's recovery from the preliminary shock would hardly have taken place. Hence the necessity of closely watching the sufferer.

Cases of prolonged collapse sometimes turn out to be trivial, while a short period of it may be the prelude to the most grave complications. The former cases are, unfortunately, rare, and profound shock of any duration should be looked upon with suspicion. This is especially the case when a second period of shock is passed through—the "relapsing collapse" of Bryant—indicative of a secondary hemorrhage or the giving way or separation of some damaged tissues.

That cases clearly showing by their history and the active symptoms a grave injury should be submitted to surgical measures as early as possible will hardly be gainsaid in the light of our present knowledge. An equally positive conclusion, based on every means of diagnosis available, will alone warrant the assertion that no serious injury is present; but, if, on the other hand, doubt exists, abdominal section will alone insure the patient adequate protection. If

nothing be found, no harm will have been done if precepts governing aseptic surgery have been closely followed; if a rent in the liver, an intestinal tear or rupture, a serious hemorrhage be discovered and adequately dealt with, the patient will have received the benefit of all our art's resources.

The seat of rupture being located, the nature of the injury will determine the procedure to follow, linear enterorrhaphy being indicated in longitudinal ruptures, and circular enterorrhaphy in complete ruptures. These procedures are now generally preferred to an artificial anus. It is sometimes impossible to adjust adequately the edges of the wound, owing to the condition of the margin, and an omental graft must be used to cover the contused area so as to avoid a secondary perforation.

Considerable extravasation of feces, blood, and other liquid or semiliquid material may have occurred into the peritoneal cavity. All chances for further contamination of the intestinal tract having thus been removed by closure of the rupture, the peritoneal cavity should be carefully cleansed by flushing with warm, sterilized water, a soft aseptic sponge being employed to mop gently all the surfaces that may, in any way, have come in contact with the infectious fluids. The cavity is then closed and free drainage insured.

Satisfactory results are obtained even in cases in which very great injury and ample opportunity for infection of all wounds have markedly compromised the issue.

The after-treatment should be based upon the necessity of insuring rest for the intestinal tract for a few days. This may be carried out by administering opiates. The patient's strength should be sustained by means of nutrient, but small and frequently administered, enemata.

Under all circumstances, an abdominal injury should cause the patient to be watched several days. After an uncomplicated injury he should remain in bed and be placed on a milk diet for a few days. **Anodyne applications** over the abdomen and a little **morphine,** internally, if there is pain, is all that is usually required in these cases. In the less fortunate the procedure to be adapted varies according to the organ involved.

Intestines.—The probability of a rupture having been recognized, the abdomen should be opened by an incision through the linea alba, and any hemorrhage quickly arrested.

The next step is to locate the visceral injury. Of importance in this connection is the fact that in the majority of cases the rupture is due to compression against the spinal column. The spot over the abdomen upon which the blow carried being considered as the one end of an imaginary line and the center of the vertebral column as the other end, the probabilities are that the rupture will be found near the linear axis.

Again, if the rupture cannot be readily found, hydrogen may be gently insufflated into the rectum, as advised by Senn, and the spot from which the gas escapes will indicate the location of the rupture,—approximately, in the case of the small intestine, and accurately below the ileocecal valve.

Disorders, or lesions other than those sought after, are misleading

conditions that should be borne in mind.

Lesions of the jejunum are sometimes difficult to locate.

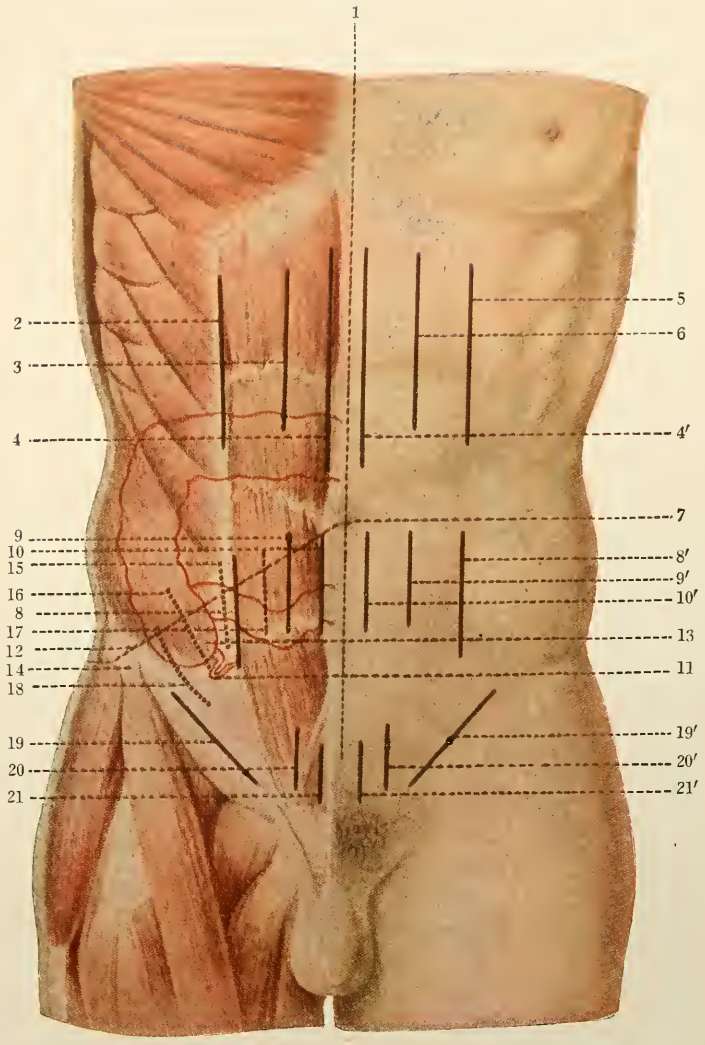
Given a case in which an injury to the abdomen occurred which is liable to produce rupture of the intestine, and the abdominal wall is found rigid and the patient suffering from pain in that region, one should not hesitate to operate, even in the absence of all other symptoms. Golden (Annals of Surg., Nov., 1906).

Two cases of rupture of the intestine successfully operated. One patient was struck in the epigastric region. Laparotomy was performed four hours after the accident and a large tear was found in the upper part of the jejunum, involving nearly one-half of the circumference of the bowel, but being placed obliquely to its long axis just beyond the duodenojejunal junction. The tear was closed with interrupted Halsted stitches and a few supporting Lembert stitches. The second patient was pinned against some railway sleepers by the arm of a crane. In this case the laparotomy was done six hours after the accident. The jejunum was completely torn through transversely in its whole circumference, and including two or three inches of its mesentery. The bowel was united with Lembert sutures. Both patients recovered promptly. Mole (Bristol Medico-Chir. Jour., March, 1907).

Diffused rigidity of the abdominal wall in a case of contusion of this region, even in the absence of any other serious symptom, is a decided indication for immediate laparotomy, while the absence of contracture, whatever may be the extent and gravity of the associated symptoms, contraindicates surgical intervention. Of 10 cases in which, owing to the presence of this symptom, laparotomy was performed, this treatment proved successful in 9. Of 17 cases of severe abdominal contusion in which no operative treatment was applied in consequence of the absence of rigidity, all ended in recovery. Hartmann (Bull. et Mem. de la Soc. de Chir., Mar. 12, 1901).

Reviews of 19 operations performed on patients who suffered from rupture of the intestine, resulting from blows upon the abdomen. Not infrequently such injury will end fatally unless immediate operation is done. The abdominal viscera, although they have no bony wall to protect them in front, are protected from injury by their position, and by the immediate involuntary contraction of the abdominal muscles which takes place the moment a coming blow is seen or expected. In injuries sustained through contests of physical strength, blows upon the abdomen are comparatively rare on account of the protected position in which the abdomen is held. The author comes, therefore, to the conclusion that, where rupture of the intestine takes place, the intestine is generally caught between the body which causes the blow upon the abdomen and one of the bony structures which form its posterior walls. F. B. Lund (Boston Med. and Surg. Jour., Nov. 20, 1905).

Stomach.—When the symptoms of complete tear are recognized, the presence of the organ's contents in the abdominal cavity render an immediate laparotomy imperative. The incision should include the tissues between the xiphoid cartilage and the umbilicus. If the tear cannot be quickly found, repetition of the inflation with hydrogen-gas will help to locate it. As soon as located any bleeding vessel should be ligated, and the stomach evacuated and cleansed through the adventitious opening of any substance that may have remained in it. If the wound be a lacerated one, it may be necessary to pare its edges. This being done, the tear is closed, the mucous membrane being united with a continuous or interrupted suture, cut short, and the muscular and serous coats by the



Lines of Incision for Abdominal Exploration and Operation (Laplace).

1, median line; 2, for liver and gall-bladder; 3, for pyloric end of stomach and duodenum; 4, 4′, for upper abdomen, including stomach and pancreas; 5, for spleen; 6, for tail of pancreas or greater curvature of the stomach; 7, umbilicus, median line; 8, 8′, 9, 9′, 10, 10′, for intestines according to location of injury, 8 being the best for appendix as it severs no muscular fibers; 11, vermiform appendix; 12, McBurney's line; 13, cecum and ileum; 14, anterior superior spinous process of the ileum; 15, 16, 17, 18, defective incisions for appendicitis: they cut across deep muscular fibers; 19, 19′, for inguinal hernia; 20, 20′, 21, 21′, for bladder according to location of injury.

continuous Lembert suture. Closure of the laceration having removed all danger of further extravasation into the peritoneal cavity, the latter must be flushed with warm, sterilized water and mopped out with a soft sponge. The cavity is then closed and a drain left if the peritoneal surfaces have been exposed to contamination for some time.

Liver.—Especially when the history of the case seems to indicate the possibility of a lesion of this organ is careful watching imperatively demanded, owing to the violent hemorrhages which they involve. Either this complication or peritonitis having been recognized, the abdomen should be opened at once in the middle line. The abdominal wound should be large enough, if possible, for the surgeon to see the liver, but in every case he ought to make a careful exploration with his finger, especially directing his attention to the convex and posterior surfaces of the organ.

When a rupture is found, the wound may either be cauterized, plugged, or sutured.

Plugging with antiseptic or aseptic gauze seems to give the best results, one end of the gauze being left out at the angle of the abdominal wound. The plug should be removed not earlier than the forty-eighth hour, lest there should be a recurrence of the hemorrhage, and not later than the fourth day, lest a biliary fistula should be formed. When the bleeding is very severe, sponges mounted on holders appear to produce more satisfactory pressure than simple plugging, which is, perhaps, better reserved for slighter injuries. Hot-water irrigation may be of advantage in these cases. A ligature should be applied to any large vessel which is seen to have been torn. Sutures are particularly useful when the laceration extends deeply into the substance of the liver, since by their means the edges of the wound may be brought lightly together and the bleeding can be controlled. Drainage of the pelvic pouch, by an opening just above the pubis, serves best to give free passage to subsequent discharges. The capsule should be included in the stitches. The prognosis is very unfavorable when peritonitis has occurred, but something may still be done to prevent the fatal issue by opening and afterward draining the abdominal cavity.

Spleen.—After a simple contusion the spleen soon returns to its normal condition without further trouble, and a few days in bed, coupled with strapping of the side to limit motion, usually suffice. When, however, there is laceration of the parenchyma the convalescence is slow, abscesses following in quick succession. After a time these cease and recovery is uninterrupted. Symptomatic treatment, revulsion over the organ, and tonics may shorten the duration of such cases.

When the symptoms do indicate that exsanguination of the patient is taking place, death will most probably follow, although the hemorrhage is not as copious as it can be in tears of the liver, the splenic capsule being more elastic than that of the latter organ. Removal of the organ should be resorted to. The abdominal wall is opened by means of an incision through the left semilunar line and the peritoneum is freely opened. The hand being introduced into the cavity, all adhesions are torn up and the

organ is brought to view. The vessels entering the hilum are then clamped and the organ is removed. The stump is ligated and, after sponging out the abdominal cavity, the wound is closed.

A study of a personal case of rupture of the spleen, and 70 cases recorded in the literature since 1891, showed that immediate operation is indicated in all cases as soon as the diagnosis is made, even though there may not be much hope of saving the patient's life. In the 70 cases referred to, 42 patients were operated on; of these, 27 lived and 15 died, a mortality of 36 per cent. All those not operated on died. The causes of failure after operation were peritonitis of other viscera, especially the left kidney; injuries of the left pleura, other injuries, such as fracture of the base of the skull, and operation performed too late. The majority of patients show no abnormal effect except a transient anemia and leucocytosis, which swings back to normal in about a month, and an enlargement of the lymph-glands, most often the left axillary and inguinal. Simpson (Lancet, Aug. 11, 1906).

Case showing that extirpation of the spleen is the best means of treating traumatic rupture of the organ. No functional hypertrophy of any other organ was observed in this case, nor any signs of disturbances from lack of functioning of the spleen. Borelius (Zeit. f. klin. Med., lxiii, Nu. 1-4, 1907).

Of the 103 cases of traumatic rupture of the spleen, reports of which have been published, the injury has been inflicted by the kick of a horse in 11 instances. In a case personally observed, treated by splenectomy, systematic examination of the blood showed that the removal of the spleen had absolutely no ill effects. Hörz (Beiträge z. klin. Chir., 1, Nu. 1, 1907).

Summary of cases of rupture of the spleen reported in literature: Unoperated: Of 220 cases, 17 patients recovered—mortality, 92.3 per cent. Operative results: Splenectomy, 67 cases, 38 patients recovered, 29 died—mortality, 56.7 per cent.; splenorrhaphy, 2 cases, 1 patient recovered, 1 died—mortality, 50 per cent.; tamponade, 6 cases, 5 patients recovered, 1 died—mortality, 83.3 per cent. In the splenectomies, 13 patients had complicating injuries, of which 9 died. In 2 which recovered, the complications were unimportant. Ross (Annals of Surg., July, 1908).

Case of rupture of the spleen in a boy of seven years who had been run over by a cart. Operation by Mr. D'Arcy Power. Chloroform was administered and a vertical incision was made 3½ inches long through the left rectus muscle above the umbilicus, 1½ inches from the middle line. The peritoneal cavity was opened and was found to contain a quantity of blood-clot and blood which was washed out with saline solution at a temperature of 110°. The anterior surface of the left lobe of the liver was found to be grazed over an area of about the size of a crown piece, but had stopped bleeding. The spleen was drawn out of the wound and was found to be badly lacerated, the lower third of the organ was almost separated from the rest, and there were extensive lacerations in the region of the hilum. The organ was held in place by a mere strand of mesentery which ruptured when an attempt was made to ligature it. As bleeding had also stopped in the spleen, some of the arteries of which were very definitely thrombosed, no attempt was made to recover and ligature the pedicle. The bleeding through the peritoneal opening had never been very free during the operation, but a drainage tube was left in the wound to be an index of possible further hemorrhage. The child came through the operation very well, and there was no further extensive hemorrhage, the drainage tube being removed on the sixth day, when the pulse had quieted down to 100. The patient made an uneventful recovery. T. S. Lukis (Lancet, June 19, 1909).

Kidney.—The majority of mild cases of perirenal extravasations of blood and urine recover as the result

of rest and expectant treatment. The patient should be kept in bed and his diet limited to liquids, the best of which is milk; this beverage requires, besides, the least physiological labor from the injured organ. The nourishment of the patient may further be sustained by rectal injections of beef-tea, and these should entirely be resorted to if there is vomiting, the latter tending greatly to encourage hemorrhage.

Details of 5 cases. The patients were men between 25 and 42, a woman of 30, and a boy of 12. Unless there are signs of internal hemorrhage, absolute repose and ice to the kidney region are indicated. The patients were all dismissed in good condition after operative intervention. Yoshikawa (Beiträge z. klin. Chir., Jan., 1909).

When hemorrhage occurs in the direction of the bladder, there is likely to be accumulation of blood-clots, which, if small, will readily pass out with the urine. Frequently, however, the clots are large and cause retention of urine and marked tenesmus. A large catheter should therefore be introduced and kept *in situ* when the hematuria is marked, and the bladder occasionally washed out with a weak **boric acid solution.** Median urethrotomy to remove clots and relieve retention sometimes becomes necessary in these cases. When the symptoms do not improve under these measures, an incision should be made, exposing the seat of injury, the extravasation removed, and the parts restored, by appropriate measures, to their normal conformation.

According to Keen, hematuria is valuable only as showing the fact of rupture of the kidney, but not as a symptom by which to decide on operating. It is not the visible loss of blood by the bladder, but the easily overlooked, but far from dangerous, bleeding into the perinephric tissues, or into the peritoneal cavity, that should receive the chief attention.

Case of rupture of both kidneys, with intraperitoneal hemorrhage, in a girl aged 16 years, who fell a height of four feet from a car, landing on her abdomen across a rail. She felt that she "had torn something loose on the inside," and, although she had some pain, she walked home, a distance of about a quarter of a mile. When seen, about an hour later, she had a temperature of 98° and a pulse of 127, with other symptoms indicating severe shock. She vomited a greenish material several times. The abdomen was distended, the right rectus rigid, the right kidney region tender, with dullness on the right side, especially in the right iliac fossa (the patient was lying on her right side). By catheter two ounces of very bloody urine were withdrawn. Intraperitoneal rupture of the right kidney was diagnosed. Owing to objections on the part of the patient and her parents the operation was not begun until about eighteen hours after the accident. She stood the operation well for the first hour, but later did poorly because of the great loss of blood. A large quantity of blood and urine was found in the peritoneal cavity, which was cleaned out and flushed with normal salt solution. The right kidney was found low in the abdomen, lying directly in front and over the third and fourth lumbar vertebræ. It showed three transverse rents and was tied at its lower pole to the left kidney by a dense fibrous band a half-inch in diameter (horseshoe kidney?). The left kidney was literally torn into fragments, entirely without a capsule, and separated from the ureter. The vessels of the left kidney were ligated and all the pieces removed. A portion of the right kidney, which had been mashed into a pulp, was removed also. The remaining portion of the right kid-

ney (not more than two-fifths of the original kidney substance) was in a very bad condition and showed two rents. It was packed with gauze. The abdomen was filled with normal **saline solution** after repeated flushings, then closed with through-and-through sutures of silkworm-gut, and drained. After-treatment for the shock was carried out. From the time the reaction set in, ten hours after the operation, the patient did well. The gauze was removed on the sixth day. A urinary sinus followed, through which most of the urine passed for the next five days. It closed on the sixteenth day. The patient sat up on the thirteenth day and left the hospital on the twenty-third day. She has enjoyed good health ever since (now more than six months) and passes a normal amount of urine. A. L. Franklin (Amer. Jour. of Surg., Oct., 1906).

The dangers of rupture of the kidney are mainly hemorrhage and sepsis. When, therefore, the symptoms are such as to indicate marked hemorrhage or sepsis, and especially if a tumor form quickly in the lumbar region, an exploratory operation should at once be done. If severe laceration be present, or the kidney's functions be practically compromised, or the hemorrhage be such as to require ligation of the renal vessels, lumbar nephrectomy should immediately be performed, primary nephrectomy being safer than secondary removal of the organ.

Bladder.—When a patient presents the history of a severe abdominal contusion or crushing, followed by inability to micturate, the catheter should at once be used.

The presence of hematuria will indicate a lesion in the urinary tract, kidney, or bladder. If the urine withdrawn is observed to be well mixed with blood and, instead of red, it appear brown and smoky, the lesion is probably one of the kidney. If, on the contrary, the urine be bright red, the probability is that the bladder has been torn. In the latter condition the diagnosis may also be assisted by the quantity of fluid passed at a given time. If, when the catheter is introduced and after a history marked with shock, no urine is obtained, the chances are that not only the bladder has been ruptured, but that the laceration is extensive, the opening having allowed the vesical fluids to escape into the abdominal cavity. A free flow, on the contrary, would tend to show that the tear, if any exist, is small. Of course, the invagination of the intestines into the vesical opening, or a valve-shaped laceration, may cause the same favorable signs to exist, thus misleading the diagnostician. Very small lesions may be present, sufficient to allow the urine to escape, drop by drop, into the surrounding parts. Detection of them is very difficult, the subsequent complications alone showing the presence of extravasated fluids.

The presence of any tear, except very small ones, may also be ascertained by injecting a weak boric acid solution into the organ, through the catheter. If a rupture be present, the bladder will not fill and rise above the pubis. Filtered air may be used for the same purpose, but it is less satisfactory, owing to the danger of secondary collapse.

The urine may have passed into the prevesical connective tissue outside the peritoneum, or the vesicorectal or vesicouterine space, owing to a rupture in these locations. This constitutes the extraperitoneal lesion. Cellulitis and sloughing rapidly ensue

without subsequent involvement of any organ in the neighborhood of the lesion, the vagina, the rectum, etc., the patient dying from septicemia.

According to Sieur, the most important signs of vesical rupture are: a peculiar pain felt at the time of the injury; chilling of the surface of the body, which persists for some time; an urgent desire to micturate, which the patient cannot satisfy; the absence of any vesical swelling above and behind the pubes, and also the absence or the presence, but in very small quantity, of urine in the bladder. Catheterizing, though valuable, ought not to be practised except with great caution.

Pathology of rupture of the bladder based on 3 personal cases and those found in literature. In many instances the rupture was not diagnosed until too late for surgical intervention. The mortality of rupture of the bladder has dropped from 43.5 per cent. in 1895 to 30.5 per cent. in 1905, when operative treatment can be instituted in time. It is especially important to bear in mind the possibility of rupture of the bladder from its being pushed down into the small pelvis by some "physiologic trauma," the attachment to the omentum tearing out a piece of the attached bladder wall where it joins the rear wall, when cicatricial changes have induced unyielding adhesions. Goldenberg (Beiträge z. klin. Chir., Jan., 1909).

To ascertain whether a tear be extraperitoneal or not, a measured quantity of a weak boric acid solution is injected through the catheter. If the full amount is not recovered, the chances are that the rupture is extraperitoneal.

Rupture into the peritoneal cavity, the intraperitoneal form of lesion, is less urgent as far as symptoms go. One, and even two, days may elapse before active symptoms appear; but, when they do, rapid progress toward a fatal issue from general peritonitis is the rule.

Uncomplicated contusion of the bladder readily yields to a few days' rest, the application of ice, and general symptomatic treatment. When, however, there is cause for suspecting a rupture from the nature of the accident or the violence of the blow, the catheter should at once be introduced. The presence of blood renders operative interference imperative. After the rectum has been distended with a rectal bag an incision three inches long is made in the middle line of the hypogastrium, beginning half an inch below the upper edge of the pubes, as in suprapubic lithotomy.

The peritoneum is then carefully rolled up, along with the prevesical fat. The bladder being thus exposed, search for the rupture is the next step. The rent is usually found along the posterior surface vertically down from the urachus; frequently an extravasation of blood and urine indicates the spot. Occasionally, however, considerable difficulty is experienced, and opening of the organ is necessary so as to permit the introduction of the finger, and thus allow of exploration of its inner surface.

The rupture may be extraperitoneal or intraperitoneal. If an intraperitoneal laceration is found, the incision should be extended upward, the peritoneal cavity opened, and the cystic wound closed with fine silk by means of Lembert sutures, one-eighth of an inch apart, including only the peritoneal and muscular coats. The mucous membrane of the bladder should be respected. Important, in this connection, is the necessity of

ascertaining that the sutures will hold; this may be done by distending the bladder with a lukewarm milk or an alkaline solution.

The abdominal cavity is then carefully irrigated and closed, leaving a drain if there is any possibility that fluids will accumulate in any of the surrounding tissues.

Henry Morris holds that there is great danger in delaying operation in these cases; the decomposition of the clots and the cystitis which is excited by their presence, as well as the frequent catheterization needed, exposes the patient to all the dangers of suppuration of the wounded kidney, and also to the risk of infection.

WOUNDS OF THE ABDOMEN.—Wounds of the abdomen may be *non-penetrating,* when the abdominal walls alone are injured, and *penetrating,* when the peritoneum is included in the lesion, irrespective of the instrument (pistol, knife, etc.) with which the lesion is produced.

Non-penetrating Wounds.—Non-penetrating wounds are usually due to pointed cutting or blunt instruments.

The lesions caused by a pointed instrument, involving the skin and muscles only, are usually very slight. With due aseptic precautions careful exploration of the wound with the finger may be resorted to if the visceral examination does not suffice. Probes had better not be used, lest the wound be transformed into a penetrating one.

Lesions caused by cutting instruments (knives, swords, etc.) vary in importance according to their depth and length. When the muscles are cut, the support for the abdominal organs is compromised, and ventral hernia may follow, unless great care be taken when the wound is closed.

Lesions caused by blunt bodies (such as shot, glancing bullets, and fragments of shells, etc.) are usually attended by symptoms of contusions corresponding in intensity with the force of the blow. Severe laceration of the abdominal tissues may thus be caused and death occur from intestinal lesions.

The hemorrhage attending these various kinds of wounds is usually slight. There is considerable ecchymosis, but this soon disappears. Occasionally shots or bullets become imbedded in the abdominal tissues.

Treatment.—After carefully arresting bleeding, cleansing, and disinfecting the wound, the tissues are united. In deep incised wounds the prevention of ventral hernia should be borne in mind, and the cut muscular tissues brought accurately together by means of catgut sutures. This being done, silk sutures are also introduced and brought out to the surface, thus including the muscles and skin. Capillary drains are alone to be used, if drainage is at all necessary, larger drains affording opportunity for the formation of a ventral hernia. The abdomen should be supported by means of a bandage applied over the dressing and the patient kept in bed until complete repair of the wound has taken place; from two to five weeks, as a rule. The bandage should be carried long after recovery, and the patient be warned of the danger he might incur by violent movement or strain.

Penetrating Wounds.—The softness of the tissues of the abdominal parietes causes them to be easily penetrated, and the organs within the

cavity are all vulnerable for the same reason. The interstices between them occasionally allow the harmless passage of a weapon or bullet, but such cases are extremely rare, only nine such cases having been recorded during the Rebellion.

The missile may graze the peritoneum and barely miss it along with the deeper organs. Unfortunately wounds causing laceration of one or more of the abdominal viscera are the most frequent, and their fatality is proverbial unless a timely diagnosis allow of prompt protective measures.

As is the case in contusions, the direction from which the missile or stab comes is of great importance. A bullet arriving from the side and striking near the linea alba would probably create a buttonhole wound or bury itself in the abdominal walls. A bullet coming from the front, on the contrary, would most probably perforate the organs in its axial line of flight. If the bullet has passed through the body an imaginary line between the entrance and exit will probably indicate the organs injured, including, of course, the peritoneum. Here again, however, the spinal column may cause deviation when the initial velocity of the bullet is small, and a deceptive line of injury furnished. To positively determine the course of a bullet is difficult in many cases.

In stab wounds the opening is frequently of a sufficient size to permit prolapse of the omentum: an evident proof that the abdominal cavity has been penetrated. This rarely occurs in bullet wounds unless a large projectile, or a bullet coming from either side of victim, has caused comparatively large solution of continuity of the tissues. Prolapse of the omentum is most frequently observed in lesions of the left side. Coils of the small intestines are also frequently prolapsed and, in rare cases, the stomach, the liver, or the spleen have appeared between the lips of the wound.

Symptoms.—As is the case after contusion, penetrating wounds of the abdomen may give rise to no symptoms capable of affording any reliable clue to the extent of the internal injuries. Profound shock may be present and no serious lesion exist.

Severely injured individuals may, on the contrary, present no acute symptoms and, perhaps, walk or ride a considerable distance before showing noticeable evidence of their condition.

Profuse hemorrhage alone gives rise to symptoms denoting a grave lesion: rapidly progressive exsanguination or acute anemia; nausea or vomiting; weak, rapid, and sometimes irregular pulse; dilated pupils; cold sweats; yawning, ending in convulsions and coma. Shock is likely to be progressive in these cases.

The only symptoms that are present in practically all cases are pallor and vomiting: the accompaniments of any severe blow on the abdomen, and therefore of no value whatever as differential signs. The temperature is of no assistance in these cases.

> In penetrating wounds of the abdomen there are absolutely no known symptoms which indicate injury to any of the viscera, except those noted in connection with the urinary tract, stomach, and occasionally the lower bowel. Except those relating to general shock, all symptoms following such wounds indicate either internal hemor-

rhage or peritonitis. To wait for symptoms of perforation of the intestines means to wait until peritonitis has developed; therefore every bullet or stab wound which penetrates the abdominal cavity should be operated on at the earliest possible moment in order to anticipate the advent of peritonitis. No time should be wasted in attempting to demonstrate the presence or absence of intestinal perforation by such means as the rectal insufflation or gases or vapors, or the analysis of recollected intraperitoneally injected air or liquids.

It is essential to systematically examine the entire gastrointestinal canal in all cases, regardless of the point of entrance of the wounding body. Whenever the alimentary canal has been perforated, suitable drains (the author prefers the so-called cigarette drain) should be placed either through the operative incisions or counterincisions, as may appear best suited to the individual case. M. L. Harris (Annals of Surg., March, 1904).

DIAGNOSIS.—On general principles dangerous complications are to be expected when marked shock, nausea, vomiting, hiccough, anxiety, intense thirst (indicating a probable involvement of the peritoneum), and insomnia are present. Besides these indications there are others peculiar to each organ which greatly assist in establishing at least an approximately certain diagnosis.

Intestines.—According to Senn, bullets striking the abdomen anteroposteriorly rarely cause more than four perforations, while oblique or transverse shots are likely to produce a much larger number of lesions: from fourteen to sixteen. On general principles, however, a penetrating wound may always be considered as having caused a lesion of the intestines.

The early diagnosis of multiple perforations is difficult, sometimes impossible. Every gunshot wound of the abdomen should be looked upon as penetrating and complicated by visceral injury, especially by wounds of the intestine, unless there is absolute proof that it is not penetrating. Whenever possible a median exploratory laparotomy should be done, without regard to the seat of the wound. The intestine should be explored systematically in its whole extent, with as little evisceration as possible. After repair of the lesion a careful toilet of the peritoneum should be provided whenever there has been a considerable escape of feces. Sourdat (Rev. de chir., xxviii, 733, 1908).

Whenever there is acute abdominal pain the possibility of perforation of some part of the alimentary canal should be considered, and the patient should not be dismissed until the possibility of such an accident can be definitely excluded. If the symptoms point rather definitely to perforation, but there is still some doubt as to diagnosis, an exploratory operation is safer than delay. Shock is no contraindication to operation, which should be as expeditious as possible, only necessary work being done and artistic ideals being left for less urgent conditions. The writer thinks that appendiceal perforation is more frequent than is generally supposed, but, as in gall-bladder perforations, there is some protection by adhesion, though unfortunately these are not always life-saving. B. B. Davis (Jour. Amer. Med. Assoc., May 14, 1910).

The most important symptom is the escape of intestinal gases and more or less fluid substances through the wound. The mere presence of emphysema around the wound is of no value, however, since air is generally forced into the wound by the bullet.

Case of a boy 14 years of age who was shot in the abdomen at close range with a large revolver. He presented an irregularly circular wound about one-half inch across just inside the

anterior superior spine on the right side. There had been very little bleeding from the wound; there was no escape of gas or fluid nor any viscus present. The abdomen was generally resistant, both flanks were dull, but the dullness was not movable. Liver dullness appeared normal. The pulse was over 160, respiration rapid and shallow, pupils dilated and expression anxious. The patient did not complain of pain and had passed clear urine since receiving the injury. The bowels had not moved. There was a good deal of shock; nevertheless the abdomen was opened immediately in the midline, below the umbilicus, by an incision about three inches long. Much blood and some fecal material of small gut consistency came away. The small intestine was delivered and almost at once a wound perforating both sides of the gut was found. Near it was a laceration on the antimesenteric side of the gut about one and one-half inches long. There was also much bruising of the mesentery between these two. The three wounds were closed in the usual way. Further examination showed seven more traumatic perforations of gut and mesentery within a distance of six feet. All this and the boy's condition made the case seem so hopeless that the abdominal opening was closed with through-and-through sutures after a large drainage wick had been placed in the lower angle extending freely into the abdomen. He was freely stimulated, given all the milk he could take and repeated large enemas. The drainage wick was removed on the second day and not reinserted. On the third day a small amount of fecal matter was passed by rectum and daily thereafter the quantity coming away naturally increased, and that by the wound decreased. With the first stool by rectum the boy's condition improved and it did so steadily and without further setback. One month after the accident the boy was up and about, and it was found that he had been eating rice, bananas, fish and cakes for ten days previously. Fysche (Montreal Med. Jour., May, 1909).

Free hemorrhage from the wound tends to indicate an intestinal lesion; if the stools also contain blood the diagnosis may be considered as certain.

Probes have been discarded in penetrating wounds, owing to the irregular course followed by the bullet in many cases and the danger of creating a false passage. Digital exploration of small wounds furnish but little information, while in bullet wounds there is danger of pushing into the peritoneal cavity what foreign substances may happen to be present.

The majority of surgeons now favor enlargement by an incision at least two inches in length, intersecting the bullet or incised wound. Layer after layer of tissue is carefully dissected on each side of the track, the walls of which, in gunshot wounds, are usually darker than the normal tissues, owing to contact with the lead or powder-products of combustion. Using the grooved director to divide the tissues and the hemostatic forceps to grasp any bleeding vessel, the peritoneum is finally reached, when the certainty that a penetrating wound is present or not may be established. If practised with strict aseptic precautions, this procedure does not expose the patient.

Stomach.—Hematemesis is a frequent symptom of penetrating wound of this organ and a much more valuable one than in contusion, since, in the latter, a slight laceration of the mucous membrane may produce it. The blood may be pure, but in the majority of instances it is mixed with partially digested alimentary semi-liquid material. If the wound is sufficiently large to allow the contents to

escape through it the nature of the injury is, of course, clear, but an important complication is to be apprehended: extravasation into the peritoneal cavity capable of causing peritonitis. If this is circumscribed, adhesions are formed and the patient recovers. Frequently, however, general peritonitis follows, ending in death. Hence the importance of an early recognition of extravasation.

Besides hematemesis and the presence of gastric fluids, there are usually present in such injuries the marked symptoms witnessed in cases of contusion: rapidly progressive anemia, pallor, fluttering pulse, etc.

> Case in which the exit hole made by the bullet in the stomach could not be found, though it had unmistakably passed entirely through it. The patient recovered normally. Research on animals has also shown that the hole made as the bullet passes out of the stomach is usually a small slit, discovered with difficulty. The entering hole is much larger and the stomach contents, if they escape at all, do so through this first opening. When the entering hole is not more than 7 or 8 mm. in diameter, it is wisest to abandon the search for the other opening if it does not readily present. The abdomen can be sutured with confidence, as the mucosa plugs the second opening. Von Frisch (Archiv f. klin. Chir., lxxiii, Nu. 3, 1904).

Liver.—A wound of the liver gives rise to all the symptoms observed when a contusion has caused laceration of the organ: Intermittent pain, radiating in various directions, especially toward the shoulder, if the convex portion of the organ is torn, and in the direction of the waist, if the concave or inferior portion of the organ is the seat of injury. There is marked pallor, superficial itching, and, later on, jaundice. The stools may be clay-colored, thus indicating the absence of bile.

The hemorrhage varies in these cases according to the cause of the lesion; one caused by a bullet is prone to be accompanied by considerable and frequently fatal bleeding. Stab wounds, when the weapon is not large, do not give rise to considerable hemorrhage. A copious flow of blood from a wound in the hepatic region indicates that the liver is involved. The flow of bile through the wound is a valuable sign, but it is seldom that this secretion can be obtained alone, blood being usually mixed with it.

> If the shock is progressive it means internal hemorrhage. When a patient is first seen he may be profoundly shocked and not be much disturbed; but if he continues to become more shocked, it means hemorrhage. Shock at the time of injury does not mean hemorrhage, but later on it does. L. McLane Tiffany (Pacific Record of Med. and Surg., Feb. 15, 1896).
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> In very severe cases the prognosis is exceedingly grave, no matter how early intervention may have been practised. Hemorrhage was the cause of death in 69 out of 162 fatal cases. Abscess and peritonitis are of course responsible for many deaths. In all probability there are many mild cases of liver laceration which go on to entire recovery without ever having been diagnosed. Of 25 cases of hepatic injury occurring in the last ten years in the New York hospitals, which were uncomplicated by serious lesions of other abdominal organs, 12 were ruptures, 9 gunshot wounds, 4 stab wounds. Eleven deaths resulted, being a mortality of 44 per cent. B. T. Tilton (Annals of Surgery, Jan., 1905).
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> The gall-bladder when distended is easily ruptured and gives rise to violent symptoms, especially if already infected, septic peritonitis being inevitable. E. J.

Senn (Jour. Amer. Med. Assoc., Mar. 23, 1907).

In some instances extensive lacerations of various organs may give rise to no preliminary morbid phenomena. Thus, W. L. Robinson reported fatal cases of marked laceration of liver and bowel in which there was neither shock, hemorrhage, nor high pulse.

Spleen.—In cases in which the spleen is wounded the diagnosis can easily be established by the location of the external opening and the direction of the track. As is the case in contusion, there is marked local pain and profuse bleeding, which, if the organ is greatly lacerated, may soon prove fatal. This is apt to occur after gunshot wounds at close range, the organ under such circumstances becoming pulpified. Puncture wounds are less likely to produce fatal hemorrhage. Pain in the left shoulder has been considered a diagnostic of value.

> Although many successful operations have been done of late for wounds of the spleen, little attention is being paid to a very valuable diagnostic sign. Case of wound of the spleen in a healthy young man in which the physician who saw the case soon after the accident made a diagnosis of simple contusion of the abdomen. The family physician who was called in a little later found, in addition to pain in the whole abdomen, severe pain in the left shoulder. Because of the increasing shock, the distention of the abdomen, the marked right-sided rigidity, and the severe tenderness in the region of the spleen, a wound of the spleen was diagnosticated. The writer first saw the patient in the evening, and agreed with the diagnosis. He was particularly impressed with the fact that the patient's chief complaint was of the pain in the shoulder. Immediate laparotomy established a wounded spleen. This organ, which was exposed with much difficulty because adherent to the diaphragm, showed two large rents, one near the hilum and the other on the convex surface. Splenectomy was performed, and three weeks later the patient was discharged cured. Pain referred to the right shoulder is very characteristic of abscess of the liver. This applies as well to the left shoulder in the case of the spleen. It is explained by the association between the phrenic and fourth cervical nerves. Levy (Zentralbl. f. Chir., Bd. xxxvii, S. 1577, 1910).

Kidneys. — Symptoms frequently accompanying wounds of the abdominal organs—extreme pallor, weak pulse, cold extremities, nausea, and vomiting—are apt to be most marked when, besides the organ itself, the peritoneum has been pierced.

A wound of the kidney gives rise to severe pain in the majority of cases, but this symptom may be absent. As in cases of laceration, the pain radiates in various directions, especially in the direction of the external genital organs. The testicle of the corresponding side, besides being the seat of considerable suffering, is frequently raised by spasmodic contractions of the scrotum.

At first a small quantity of bloody urine may be passed, but this is often followed by vesical tenesmus and complete retention, due to the presence of clots in the bladder.

Much information is sometimes obtained by a close examination of the wound of exit. If the track of the bullet be anteroposterior and the missile have entered from the front and penetrated the kidney, the exit wound will be found in the lumbar region. It is frequently found in this situation to contain urine, a positive indication that the organ or its annex, the ureter, has been wounded.

The diagnosis of gunshot wounds involving the kidney may sometimes be made from the objective signs of injury of the kidney; in other cases the symptoms will be those of shock and intra-abdominal bleeding, as in stab and incised wounds. The cardinal signs are hematuria and the escape of urine from the external wound. Owing to the narrow wound of entrance, this latter sign is much less common in gunshot injuries.

If either ureter is plugged by a clot, severe renal colic may be present. In gunshot wounds involving the abdominal viscera, operated in for the control of bleeding or for the repair of wounds of the hollow viscera, it will be rare that the surgeon can diagnosticate injury of the kidney before opening the abdomen, unless hematuria or kidney colic have existed. Johnson (Annals of Surg., Oct., 1909).

If the wound of entrance be in the back, its location over the site of the kidney may suggest a lesion of the latter; but the urine test will only be of value if the projectile only penetrate the kidney without perforating it.

If it penetrate the organ, the extravasation will take place into the peritoneal cavity. The same will be the case if the missile enter from the front without going through the organ. Bullets buried in the renal parenchyma either become encysted or cause abscesses, and pass out through the ureters or into the adjoining parts.

Bladder.—The symptoms vary according to the location of the wound. A perforation between the symphysis and the peritoneum above does not give rise to general symptoms; whereas shock, pallor, weak pulse, vomiting, etc., may be much marked when the peritoneum is involved in the injury. In all cases, however, severe pain is experienced at the site of the lesion and radiating to the thighs and testicles.

The passage of urine soon becomes very difficult and spasmodic. It may be voided, drop by drop, for a long while, notwithstanding the efforts of the patient, then suddenly gush out for a few moments and again flow slowly. This symptom may be due to accumulation of clots or to spasm of the urethra. If the catheter is passed, hematuria becomes evident when the bladder has been penetrated: a characteristic sign.

As in the case of rupture due to contusion, infiltration may take place through the wound into the neighboring tissues; any obstacle to the free passage of urine greatly encourages this. Hence the necessity, in all bladder lesions, of keeping the organ as free as possible by the frequent use of the catheter.

Two important clinical features present in cases of traumatic ruptures of the bladder that are not noted by the classical authorities: (1) The persistent uniform capacity of the bladder, and (2) the manner in which the bladder may be refilled after complete evacuation by the catheter. The first is explained by the fact that the rupture is situated in the upper part of the bladder, the lower part of which still acts as a reservoir. When the urine reaches the level of the rupture it escapes into the abdominal cavity. Repeated catheterization will, therefore, withdraw each time about the same quantity of urine, but it does not influence the urine in the abdominal cavity. The second symptom is due to a change in position from the recumbent, in which the urine is evacuated by the catheter, to the upright, in which the bladder is immediately refilled by the urine which has escaped through the rupture into the lower part of the abdominal cavity, and which now as readily returns to the bladder, as shown by cadaveric experimentation.

Two etiological factors were noted in these cases, the tolerance of the bladder, which can be distended to the point of rupture, and the degeneration of the muscle which causes a diminished resistance to distention. Morel (Annales des mal. des organes genito-urin., June 1, 1906).

PROGNOSIS.—The statistics so far published differ so widely that it is difficult to reach a definite conclusion. It is certain, however, that gunshot wounds are more frequently fatal than stab wounds, but that stab wounds, in which the peritoneum is penetrated, are fully as fatal as gunshot wounds.

The kind of weapon inflicting the injury plays an important rôle in this connection. A triple-edged bayonet is more likely to produce a serious laceration than a flat blade. Again, wounds caused by small weapons, such as a Flobert rifle, for instance, would hardly produce lesions to be compared to the old Enfield or Minie rifles, which sometimes caused a large portion of an organ to protrude through a wound of exit the size of an apple.

Portions of the solid viscera are sometimes cut off or shot off, leaving a gaping tear, which greatly compromises the issue. Again, as is often the case with the liver, the bullet, or any foreign material dragged in by the latter, may lead to complications which greatly reduce the chances of recovery.

An important factor is the time elapsing between the receipt of the injury and that at which competent treatment is applied in mild cases. This is especially true as regards the early utilization of surgical measures when these become necessary. The sooner these are instituted, the more favorable the prognosis, especially during the first ten hours.

The relation between spontaneous cures and operative interference as worked by Eisendrath in 1902 is about as follows:—

Spontaneous Recoveries.

	PER CENT.
Spleen	15.8
Liver	21.8
Intestines	7.
Kidney (extraperitoneal)	70.
Kidney (intraperitoneal)	0.
Bladder (intraperitoneal)	2.
Bladder (extraperitoneal)	11.

Operative Recoveries.

PER CENT.	
56.	(50 cases).
59.5	(37 cases).
48.	(42 cases prior to 1896).
50.	(38 cases since 1896).
80.	
100.	(6 cases).
52.	(43 cases).
30.	(last 15 years).—Mitchell.

Hence the need of abandoning our policy of expectancy and delay and to recognize our duty as soon as even a probable diagnosis of rupture of one of the abdominal viscera without external signs has been made. Rather a few laparotomies in vain than allow the former mortality rate to continue.

Intestines.—The prognosis depends greatly upon the nature of the lesions. Stab wounds opening the intestine lengthwise, if small, often heal of their own accord; transverse wounds are more serious, while complete section of the bowel is a very dangerous complication. Gunshot wounds show a great fatality. Prior to the introduction of antiseptic surgery the mortality exceeded 90 per cent.; since then, the mortality has been decreased to 43 per cent. in cases operated during the first twelve hours.

When all surgeons will handle the intestines with gentleness, operate quickly, and otherwise reduce the chances of shock, it is probable that the prognosis will be greatly improved. Perforations of the descending colon and sigmoid flexure are seldom fatal; those of the transverse colon give a worse prognosis, by the formation of fistulæ, adhesions, and abnormal communications. Again, diathetic conditions may compromise recovery.

Notwithstanding great injury and other conditions greatly reducing the chances of recovery, recoveries are occasionally obtained.

Statistics collected by various writers, according to Conner, showed the mortality to range from 65.6 per cent. to 70.67 per cent. Shock is one of the chief causes of these results.

> Case of a penetrating wound of the abdomen in which there were 19 perforations in the small intestines, besides a number of wounds in the mesentery. Operation was performed on the day following the injury, and fifty-one days afterward he was perfectly well. Iden (Medical Record, Nov. 18, 1905).

Stomach.—Uncomplicated wounds of this organ frequently yield without trouble when the bullet, blade, or other instrument causing the perforation is small, especially if the stomach was empty at the time the injury was inflicted. The mucous membrane bulges out and forms a plug which obturates the hole until reparative processes have sealed the aperture on the peritoneal side. Complicated cases, in which the lesions are extensive, soon reach a fatal issue if deprived of timely surgical intervention.

Liver.—The prognosis of wounds of the liver depends mainly upon the complications. If the patient does not die from hemorrhage soon after the receipt of the injury, he is still exposed to the results of extravasation into the peritoneal cavity, the presence in the liver of a foreign body,—the bullet and what material it may have forced into the wounds,—etc. Peritonitis, hepatitis, and abscess are, therefore, dangers to be taken into consideration. Hepatitis and abscess are much less to be feared, however, from stab wounds, no foreign body being left behind, unless, as in dueling, the sword-point strike the spinal column, causing the blade to break. In such an event, however, the hemorrhage would probably prove mortal very rapidly.

As to mortality, the statistics of Edler, Mayer, and others show it to average about 50 per cent., including the cases attended by complications.

Spleen.—Slight punctured wounds of the spleen are not mortal unless complicated with laceration of a large artery. They are sometimes followed by abscesses which heal after a prolonged period in the great majority of cases. Severe punctured wounds are dangerous in proportion, but, if the primary hemorrhage is not such as to cause an early fatal issue, the chances of recovery are about those of slight wounds.

Gunshot wounds are much more serious as a result of rupture of the spleen taking place under the concussion. When the bullet is large and its velocity is great, fatal hemorrhage quickly ensues. Rupture of the spleen may also occur during convalescence.

During the War of the Rebellion the proportion of deaths was 93 per cent. In civil life, however, the weapons used are, as a rule, less

powerful, and it is probable that the mortality, especially since antiseptic surgery has been generally utilized, is much smaller. The predilection of this organ for abscess greatly darkens the prospects of recovery.

Kidneys.—Complications are also to be feared in lesions of this organ, namely: peritonitis, nephritis, and secondary hemorrhage. Again, the position of the kidney makes it probable that other organs are also injured in the majority of cases. The direction from which the bullet or stab came, the length of the penetrating blade, etc., are important factors when the nature of the injury is to be determined.

Bladder.—Gunshot wounds of the bladder are always serious as far as complications are concerned, rectal, vaginal, perineal, and scrotal fistulæ being very frequent.

As to the mortality of penetrating wounds of the bladder, it is not so great as in lesions of any of the other abdominal organs. Stab wounds are more frequently mortal than uncomplicated bullet wounds, the proportions being 29 per cent. in the former and 17 per cent. in the latter. When, however, osseous lesions are also present, penetration or fracture of the pelvis, etc., the mortality reaches 29 per cent.

> Injuries of the bladder are most frequent in males, owing to greater exposure, and perhaps to anatomic causes. Distention is one of the main factors: an empty bladder is rarely injured, except with fracture of the pelvis. The majority of bladder tears are intraperitoneal, and rapid progressive peritonitis results unless prevented by radical surgery. Virulent sepsis follows the extraperitoneal rupture. E. J. Senn (Jour. Amer. Med. Assoc., Mar. 23, 1907).

TREATMENT.—The preliminary measures indicated in the treatment of complicated contusions of the abdomen are also applicable in that of penetrating wounds of that cavity. Protrusion of portions of the intestines, the mesentery, and the omentum through the external wound is an early complication met with in many cases of penetrating wound. If the protruding mass be intestinal and in good condition it should at once be returned into the abdomen. An easy way of accomplishing this (recommended by Levis) is to raise the middle of the patient's body by means of a pillow, the hands, etc., while he is lying on his back. The anterior portion of the pelvis is thus separated to an abnormal degree from the anterior portion of the thorax, and the increased room in the abdominal cavity thus obtained causes the intestines to spread out, as it were, and, their weight causing traction upon the protruding loop, the latter quickly slips in.

At times the accumulation of gas or fecal matter checks its inward progress; the gas can easily be let out by inserting a clean hypodermic needle into the projecting bowel; the fecal matter can also be reduced in quantity by drawing out an additional portion of the gut—thus increasing the size of the loop—and gently pressing small portions of the contents into the unprolapsed bowel, thus diminishing the tension of the protruded mass. It is sometimes necessary to enlarge the abdominal wound. If the projecting mass be greatly inflamed the latter procedure is unavoidable. If it be gangrenous it had better be incised and the formation of a fecal fistula permitted.

To obtain a closure that will prevent hernia and protect the abdominal wound against infection, the writer recommends the following method: The ordinary "gridiron" operation is done, and the peritoneum is then caught up and incised in the line of the skin incision; each side of the peritoneal wound is then drawn out and sutured to the skin on both sides with a running suture of catgut or a few interrupted sutures. Retractors may then be put in and the adhesions broken up and the appendix removed; one or two small drains are now placed, and each end of the incision closed around them by means of one or two through-and-through silkworm-gut sutures. To insure better approximation of the deep layer of muscles a silkworm-gut suture may be placed on either side of the skin incision before the peritoneum is opened, and left to be tied when the operation is completed. Torrance (Therap. Gaz., Jan., 1909).

An omental protrusion, if healthy, can be immediately returned, but if greatly inflamed or gangrenous it should be transfixed near the abdominal wall and tied with a double ligature; then excised. The stump is then secured in the deeper portion of the wound with ligatures and adhesive strips.

Punctured wounds of the abdomen are frequently recovered from spontaneously, owing to the absence of serious visceral lesions. The same statement may be made as regards bullet wounds, but with less emphasis. That laparotomy should be performed in every case is a view that widespread clinical testimony does not sustain; but that a wound of sufficient importance to cause anxiety be enlarged down to the peritoneum to allow of a careful examination and adequate procedures, if need be, and that laparotomy proper should be reserved for lesions which, from the nature of the symptoms, tend toward a fatal issue, are in keeping with the teachings of the most advanced, but safe, surgery.

Active operative intervention, when admitted by the general condition of the wounded, and the surrounding circumstances, is indicated in all cases of perforating wounds of the abdominal cavity, with the exception of wounds inflicted with the modern small-caliber undeformed rifle bullet. In these cases expectant treatment gives the best results. All those wounded in the abdomen need full rest, at least for one week after the infliction of the wound. Wreden (Military Surgeon, March, 1907).

Case of extensive gunshot wound caused by the accidental discharge of both barrels of a shotgun in contact with the body. The contents of the two barrels struck the abdomen at and above the left superior spine of the ilium, and came out at and above the iliosacral joint, tearing away all the soft tissue from the crest of the ilium and the crest itself, above a line drawn from a point one inch back of the anterior superior process, around the outside of the bone to the upper limit of the sacroiliac joint. The joint was not entered, but two transverse processes of vertebræ were blown off and many pieces of detached bone were scattered throughout the soft tissues. The peritoneal cavity was entered, exposing the sigmoid flexure, the lower pole of the left kidney, and the anterior end of the floating rib. It could not at first be determined whether the sigmoid was perforated or not, but in one or two days leakage of gas showed that it had been injured. The lumbar muscle was practically destroyed. As there were no signs of serious hemorrhage and it was recognized that the wound had been practically sterilized by the burning of the discharge, the attending practitioner wisely refrained from overmuch probing or interference, merely removing loose and dead tissue, clothing, etc., and applying a sterile dressing. In about two weeks the pa-

tient was taken by train to New York, about 1000 miles. There it was found necessary to remove the anterior part of the crest of the ilium, which had become denuded of periosteum, and other portions of embedded bone that were found, and zinc plaster was used to narrow the wound. Another operation was performed four months later, anastomosing the under surface of the transverse colon, between the mesocolon and omentum at the junction of the middle and left third of the mesocolon with that portion of the sigmoid which could most easily be brought into apposition. A fourth operation was undertaken, still a year later, to close the intestinal opening and furnish a parietal peritoneum, against which the intestine could rest, thus minimizing chances of adhesion and protecting against ulcerative processes in the exposed intestinal area; to find an external covering for what must be a large hernia, and to devise a means for controlling its extension and future enlargement. The patient, at the time of report, two years after operation, was in excellent health, able to perform all the duties and functions of life, walking four or five miles a day for recreation. Polk (Abstract in Jour. Amer. Med. Assoc., from Med. Rec., Apr. 18, 1908).

In all penetrating wounds of the abdomen seen within twelve hours of the injury, operation should be done promptly. The incision should be large enough to insure a thorough survey of the abdominal viscera without unduly exposing them. Extensive evisceration is unnecessary and unjustifiable, greatly increasing the mortality. Unless the peritoneum is extensively soiled, intestinal contents should be wiped away with salt gauze sponges, irrigation doing more harm than good. If the closure of the perforation or destruction of blood-supply threatens seriously the usefulness of a portion of the bowel, resection should be done. If the peritoneal cavity is generally or extensively soiled, or if there is any considerable oozing, drainage is safer; otherwise, the incision may be closed.

Postoperative treatment is very important. If there is no lesion in the large bowel salt solution and coffee, of each, 150 c.c., should be given per rectum every four hours. Branch (Annals of Surg., Aug., 1911).

When surgical measures become necessary, including enlargement of the wound, the patient should be placed under an anesthetic. The rectum should be emptied by copious injections containing a tablespoonful of glycerin to the pint. A subcutaneous injection of morphine (¼ grain) is recommended by many surgeons. If, however, there is a tendency to shock without much pain, this agent had better be withheld. Rectal injections of whisky and warm water, 2 ounces of the former and 4 of the latter, is useful to sustain cardiac action. It may be repeated in an hour if evidences of impending shock are still present.

If, after a careful examination of the enlarged wound, it is found that the peritoneum is not involved, the exposed tissues are carefully cleansed and the wound is closed, deep sutures being used to hold the tissues in accurate apposition. As already stated, the possibility of ventral hernia should be borne in mind: the patient should be kept in bed for some time and a bandage be worn until all local weakness has disappeared.

If, after a stab wound, the parietal peritoneum alone is found incised or penetrated and there is no evidence that the organs behind have suffered injury, the tissues must be cleansed with great care and the peritoneal flaps brought together, the serous surfaces being kept in contact. A continuous catgut suture is used for the peritoneum; the muscles and skin

are then united and the wound is closed. The measures already outlined to prevent ventral hernia are also indicated for the deeper wound.

When laparotomy becomes necessary the incision should be made in a spot affording the operator the greatest opportunity for a wide field of action, and should be sufficiently long. When performed for the arrest of dangerous hemorrhage, a long median incision will enable the surgeon to reach any organ with ease: an important factor, for the missile or blade inflicting the injury may have traversed harmlessly between several coils of intestine and have caused a rent in the organ most remote from the point of entrance. Again, the incision should be free, so as to make it possible to easily reach all parts of the abdomen to allow of a thorough removal of all extravasations which might otherwise ultimately cause complications.

As the late Nicholas Senn taught, one of the important elements of success in the treatment of gunshot and stab wounds of the stomach is time. Unnecessary time lost in finding and suturing the visceral wounds is a source of immediate danger to life which should be eliminated as far as possible by means which enable the surgeon to make a quick and correct diagnosis, and by resorting to a method of suturing which closes the wound safely and securely with the least possible delay, and which leaves it in a condition most favorable for speedy definite healing. It is well known that small penetrating wounds of the stomach often heal without operative intervention. By contraction and relative displacement of the different muscular layers of the thick wall of the stomach the tubular wound is contracted and obstructed sufficiently to prevent leakage until the canal on the peritoneal side becomes hermetically sealed by firm plastic adhesions which prevent extravasation during the time required for the repair of the visceral wound. If in larger wounds of the stomach the same degree of occlusion can be accomplished by the simplest mechanical means, then such a procedure should take the place of the more time-consuming methods of suturing now in general use. This can be accomplished with the purse-string suture.

In gunshot injuries the defect in the stomach-wall is circular and the wound-margins contused; hence the deep sutures could at first furnish a barrier to the escape of stomach-contents only for a short time, as their hold in the necrosed tissues would be imperfect and only of brief duration. In short round wounds the circular suture is the one which will bring and hold together in permanent uninterrupted contact the serous surfaces in the most efficient manner. In the treatment of gunshot wounds of the stomach the principal object of suturing should be to close the perforation in such a way as to guard securely against extravasation, and at the same time approximate and hold in apposition a maximum surface by intact healthy peritoneum. This is accomplished by making a cone of the injured part of the stomach with the apex corresponding with the wound directed toward the lumen of the organ. The purse-string suture applied in the manner that will be described in the experimental part of this paper will maintain this cone

until the healing of the visceral wound has advanced sufficiently to render further mechanical support superfluous. The cone on the mucous side of the stomach acts in the manner of a valve, which in itself is an effective barrier against the escape of stomach-contents, while the circular suture constitutes almost an absolute safeguard against leakage, and brings in contact the serous surfaces in the interior of the cone. For wounds of the posterior wall of the stomach the author recommends a purse-string suture of heavy durable catgut to be applied through the anterior wound. The anterior wound is closed with a purse-string suture of silk of medium size applied to the base of the cone on the serous side. It is desirable that the circular suture should cause no necrosis of the included tissues. By using an absorbable suture in closing the posterior wound in the interior of the stomach this object is gained, as only a small part of the thickness of the stomach-wall is subjected to pressure, and the tension caused by the ligature is gradually lessened by softening of its material, and is entirely removed by the absorption and digestion of the ligature in less than three weeks.

The wound of the posterior wall of the stomach is found and made accessible by inserting through the anterior wound a grasping forceps with which the posterior wall is seized at a point where, from the course of the bullet, the second wound is supposed to be located. Through a wound large enough to admit the index finger the greater part of the posterior wall of the stomach can be made accessible to sight and touch, and the perforation can be located and closed with the purse-string suture in a few moments. In doubtful cases inflation of the stomach should invariably be practised for the detection of a second and possibly a third perforation.

The experiments demonstrated the safety of the circular suture in the treatment of gunshot and other penetrating wounds of the stomach. All of the animals operated upon in this manner recovered and the repair of the injuries as shown by the specimens are ideal. The absence of adhesions over the posterior wound and their constant presence over the anterior wound indicate that the presence of the silk ligature and the needle punctures were the causes of the circumscribed plastic peritonitis which produced them. In none of the specimens could any indications be found of necrosis of any of the inverted tissues, and included in part by the circular suture.

In the course of three weeks the continuity of the mucosa at the seat of the injury was completely restored. The result of these experiences has convinced the author that the circular suture compares favorably with the methods of suturing in general use, and besides has the great advantages over them in the case of its application and the saving of much valuable time.

Suturing of the posterior wound by partial eversion of the stomach through the anterior obviates unnecessary handling of the organ and the necessity of interfering with the vascular supply incident to exposure of the posterior wound, as is done by the methods most generally practised. If extravasation into the retrogastric space has taken place, flushing through the posterior wound and a

vertical slit in the gastrocolic ligament and gauze drainage through the latter are invariably indicated. (N. Senn.)

The stomach and the transverse colon are best brought to view by an incision through the rectus muscle. In the case of the stomach hernia of the mucous membrane will facilitate recognition of the lesion. The ascending colon requires lateral incision on the right side, and the descending on the left. These also should be sufficiently long to facilitate the search for the injury or injuries that may be present in the organ itself and beyond.

The incision may be such as to intersect the wound of entrance. This is desirable at all times, the aim being, of course, to always avoid unnecessary solutions of continuity. Such an incision can fortunately be made in many of the cases in which the hemorrhage is not formidable.

Hemorrhage.—When the abdominal cavity is opened and the hemorrhage, which is usually more venous than arterial, is marked, the blood rapidly accumulates in the most depressed portion of the cavity from an invisible source. To mop out the blood with sponges is generally recommended; but such a procedure does not cause the hemorrhage to cease,—the first *desideratum*. In these formidable cases an assistant should at once introduce his hand through the wound—hence the advisability of a long incision—and compress the abdominal aorta below the diaphragm. This procedure immediately checks the flow.

> Six personal cases of injury of the liver in which is emphasized the value of controlling liver hemorrhage by suture, making the peritoneal toilet by dry sponging instead of irrigation, and the avoidance of package and drainage. J. E. Cannaday (Lancet-Clinic, Nov. 10, 1906).

If any difficulty is experienced, the digital pressure upon the aorta may, for an instant, be decreased, and a sudden gush will point to at least the direction from which the blood comes. The necessary steps are then taken to arrest the flow, and the abdominal aorta is released as soon as possible,—not suddenly, but by a gradual reduction of pressure.

The measures to be employed in arresting hemorrhage vary according to the organ involved. Gunshot wounds of the liver are frequently stellate, and rents, radiating from the bullet-track in various directions, greatly increase the bleeding surface, the parenchyma in this organ taking part to a great degree in the emission of blood. To force resilient sponges into these tears is to increase their depth. If the wound be not very extensive, it may be sutured with catgut or cauterized with the actual cautery. If the wound is extensive it had better be packed with long strips of iodoform gauze, one end of which is brought out of the external wound.

> The modern tendency in wounds of the liver is toward early laparotomy. Open wounds should, without exception, be treated by enlargement of the wound, exposure of the liver, and determination of the site and extent of the injury. Care should be taken to examine the entire liver, as a second wound may remain unnoticed and give rise to fatal bleeding. The best methods of stopping hemorrhage are by the use of sutures or gauze packing. If the former are used they should include considerable liver tissue at the edges of the wound and, if possible, go down to

its full depth. Gauze packing is particularly suitable for contused wounds, gunshot wounds and punctured wounds, and is, furthermore, a useful addition to suture. The thermocautery is of very little value in arresting hemorrhage from the liver. The blood and bile can easily be removed by flushing the abdomen with hot saline solution or by dry sponging. Drainage is employed in subcutaneous wounds chiefly for the purpose of arresting hemorrhage. Tilton (Annals of Surg., Jan., 1905).

When the intestinal injury and intraperitoneal hemorrhage occur together and the blood is extravasated more quickly than the intestinal contents the hemorrhage acts mechanically, and perhaps also by its protective power, to encapsulate the peritonitis. The hemorrhage will be brought to a standstill more quickly by the tension of the abdominal walls, the flatulence, and paralysis of the intestine when a mesenteric vessel at its juncture with the intestine is injured. An intraperitoneal hemorrhage may thus act to reduce the threatening danger of an injury to the intestine under favorable conditions. Gutzeit (Münch. med. Woch., June 29, 1909).

The spleen is next in order as to profuseness of hemorrhage. The same procedures may be adopted as for the liver, but the introduction of iodoform strips is to be preferred. If these means fail, splenectomy is the only measure left.

Particulars of 3 cases of injury of the spleen, bullet wounds in 2 and laceration in the other case, which terminated fatally from internal hemorrhage. The spleen was removed in the other patients. One was a man of 66, and the remarkably slow recovery was a noticeable feature. It seemed as if the lack of regeneration of the blood from the absence of the spleen retarded convalescence. An accessory spleen was found in the other patient, a young man of 27, and his prompt recovery may have been facilitated by the presence of this compensating organ. Graf (Münch. med. Woch., lii, Nu. 44, 1905).

The writer has collected 70 cases of rupture of the spleen recorded since 1891, which are reported with sufficient fullness to admit of some comparison. From the standpoint of treatment there are four groups of cases: (1) those in which the patients die at once or within a few minutes of the accident—which hardly come within the range of surgery, as no case of successful operation has been done within the first hour; (2) those in which the symptoms are delayed from twenty-four hours to fifteen days; (3) those—the majority—in which, after the initial shock of accident is recovered from, symptoms of hemorrhage appear within one to twenty-four hours; (4) the few cases in which the symptoms of rupture of the spleen are present which gradually recover without operation. All of these patients should be operated upon. G. S. Simpson (Lancet, Aug. 11, 1906).

Tears in the spleen cause hemorrhage. This may be slight and cease spontaneously. But it may go on until the patient has become dangerously anemic. At times operation is done on such cases, and it is found that the bleeding from a tear in the spleen has stopped, or at most requires a small plugging with iodoform gauze. In other cases the tear may be so large that no other means are left than removal of the organ. This must be done without hesitation. O. Hildebrandt (Berl. klin. Woch., Jan. 7, 1907).

Sometimes a portion of the organ projects through the wound; removal of the protruding portion should be practised after passing a ligature around the mass.

The walls of the stomach and intestines may also give rise to marked hemorrhage notwithstanding their comparative thinness. The number of vessels coursing through them, however, is very great. In these

cases it is best to hem the margins of the wounds with fine silk. The bladder may be treated in the same way.

The mesentery sometimes bleeds profusely when perforated. The mesenteric vessels should be ligated *en masse* with fine silk.

Hemorrhage of the kidney is arrested in the majority of cases by iodoform-gauze package. If this should prove ineffectual the organ must be exposed and the vessels tied if possible. If not, nephrotomy or nephrectomy should be resorted to. The latter operation does away with the chances of complication attending the former, while the kidney of the other side assumes the function of both.

Injuries to the kidneys are common. At times one or two small tears may be seen on the surface, or the tears may be deep; and again, the whole organ may be crushed into two parts. The kidney is usually crushed against the first lumbar vertebra. The first class of case shows a short lasting hematuria, but no anemia, while if the tears are deeper the hemorrhage may last for some time. In the case of a completely torn organ one finds very extreme anemia, great pallor, cold clammy skin, and restlessness. The abdomen is excessively tender, the pulse is thready, and the impression is obtained that the patient is dying rapidly from loss of blood. If the abdomen is opened, huge effusions of blood are found, and in the midst of the blood the kidney lies buried. One only has a short time during which one can still save the patient. For the first two classes one waits for matters to develop, but in the third class one must operate and remove the kidney at once. O. Hildebrandt (Berl. klin. Woch., Jan. 7, 1907).

Four cases of rupture of the kidney treated conservatively, rather than by nephrectomy. The abundant literature of the subject shows that the advantage lies with conservative treatment. Surgical interference should aim to control hemorrhage and prevent extravasation of blood and urine into the tissues and abdominal cavity, also to treat other organs which may have been injured simultaneously, and, finally, to place the injured kidney under conditions which shall be most favorable for repair, including the providing of means against the occurrence of infection. An operation, if indicated, should not be delayed. The injury is so slight in many cases that an operation is not required. The conditions must be carefully weighed to decide between an abdominal or a lumbar incision. Neilson (Amer. Jour. Med. Sci., Jan., 1908).

The tampon should be employed in those cases in which there are no immediate signs of injury of the kidney or in which these signs come on slowly. In these cases we may consider that the lesions are benign and the hemostasis due to spontaneous clotting. Bleeding may, however, occur later in these cases, from the withdrawal of the tampon or the separation of a slough. Of 6 cases of nephrectomy for gunshot wounds of the kidney, 3 recovered and 3 died. Anuria is due in the greater number of cases to a reflex inhibition, produced by the trauma of the injured kidney upon its fellow, and signifies only an important lesion of the renal parenchyma. The coexistence of a wound of entrance in the lumbar region is an indication for an exploratory incision. Clement (Ann. d. mal. d. org. gen.-urin., p. 1281, 1909).

Perforation.—The fact that the intestines are, at times, perforated in twenty spots by a bullet suggests the considerable degree of care that should be given to this part of the procedure, which is carried out in the following way: The perforation nearest the rectum having been detected, the portion of intestine perforated is gently brought into full view. An assistant causes the gas in

the portion of gut below the laceration to escape through the latter by slight pressure. This being done, the next step is to ascertain whether there is another perforation above. A fresh, aseptic glass tube is placed at the end of the insufflating tube and introduced into the wound with the tip directed away from the rectum. The assistant now being directed to compress the intestine below the perforation, a small amount of gas blown above the latter will inflate the upper segment if there is no opening, or indicate the location of the perforation if there is one. As soon as the latter is detected, the tube is withdrawn, the neighboring intestine on each side of the first perforation is disinfected, and the opening is closed. This procedure is renewed until all perforations have been found and closed. This plan renders unnecessary the removal of the intestines from the abdominal cavity during any part of the operation, the source of complications in many cases, and of death by aggravated shock in others, and is now recommended by the majority of American surgeons.

> Case of a man aged 28 years, who was accidentally shot in the abdomen in the region of McBurney's point, with a 32-caliber revolver. About four hours later the abdomen was opened in the median line and was found full of blood. Nineteen perforations of the small intestine were discovered, as well as several wounds of the mesentery. At one place there were five perforations in four inches of gut, necessitating resection. End-to-end anastomosis was done, using the Cushing suture, and the other perforations were closed with purse-string sutures. The intestines were cleaned with gauze, wet with hot salt solution, and the wound closed without drainage. The operation consumed two and one-half hours, and at its close the pulse was imperceptible at the radial, facial, and temporal arteries, and the heart beats were from 170 to 180 a minute. In spite of the grave condition of shock, the patient rallied very quickly, and the wound healed by primary intention, the man returning to his work, perfectly well, fifty-one days after the operation. Iden (Med. Rec., Nov. 18, 1905).

There is great ground for the objection to Senn's method, made by many surgeons, as regards its use for purposes of diagnosis prior to laparotomy, but, in the detection of perforations after the abdomen has been opened, it is of value, and may be used, at times, to great advantage.

The manner of closing the wound is that indicated for lacerations following blows. The stomach and intestinal perforations being treated in the same way, the margins of the wound are turned inward and the serous surfaces are united by a continuous, fine-silk Lembert suture or by interrupted sutures, including the serous and muscular coats and the submucosa. These are cut short and left in, being eventually discharged *per anum.*

At times the tissues around a perforation are sufficiently contused to render an omental graft necessary.

Enterectomy is sometimes required, and not infrequently exsections of the intestine are necessary. In that case the intervening portion, if it is not too long, had better be resected, thus avoiding a double operation in the continuity of the gut.

After the active measures described have been carried out the extravasation of the contents of the stomach or intestines may make it necessary to flush the peritoneal cavity. Warm, sterilized water should be used, but

care should be taken not to handle the intestines roughly. By turning the patient on his side the fluid is poured out. The abdominal cavity is then dried with large sponges wrung out of warm, sterilized water. Chilling of the viscera should be carefully avoided, and the parts should be exposed to the air as short a time as possible.

Drainage is sometimes necessary, especially for wounds of the solid viscera, such as the liver, spleen, kidneys, etc., in which active meas ures were not resorted to early. The weight of evidence, however, stands in favor of dispensing with drainage whenever it is possible.

> Whenever the muscular wall is rigid, no time should be lost before operating, or at all events seeking the assistance of the surgeon. The rigidity is due to beginning peritonitis, which is well marked within two and a half hours of the injury. If one operates in severe cases early one can obtain much more favorable results than one used to get when one waited for the signs of peritonitis to develop. Out of 12 cases of intestinal injury, the writer saved 5 by operation. O. Hildebrandt (Berl. klin. Woch., Jan. 7, 1907).
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> Previous to 1890 few cases of intestinal rupture were treated surgically, and the result was usually a fatal one. From 1894 to 1904 there were 32 recoveries reported in English, American, French, and German literature. Though the accident is relatively rare, it is not infrequent in occupations in which traumatism by squeezing is of common occurrence. Lumbermen and coal miners are exposed to such accidents. Rupture usually occurs where the motility of the gut is restricted by a short mesentery. The omentum usually escapes serious injury, while the mesentery undergoes injury similar to that which is sustained by the gut. Conditions are more favorable for an operation when the accident occurs several hours after a meal. Golden (Annals of Surg., Nov., 1906).
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> If the intestine is perforated and not repaired the patient will die. The instrument inflicting the operation is not a matter of much moment. Prompt and immediate operation is imperative. It is undesirable to probe or unnecessarily manipulate the wound with the object of cleansing it. Excluding wounds of the abdominal region and those which give rise to dangerous hemorrhage, or pressure of the brain, and finally those in which the position of the bullet is clearly made out and its removal is not fraught with danger, simple aseptic dressing and awaiting developments is unquestionably the best policy. Of course, where bones are broken the ordinary treatment of bone fractures is in order. Shiels (Amer. Jour. of Surg., Aug., 1908).

To summarize: we will say that immediate exploration of the abdominal cavity is indicated as soon as it is suspected to have been penetrated or in any way injured by a traumatism. The injury to its contents must then be repaired under strict aseptic precautions. The value of **salt-solution flushing** is emphasized by the results of practical experience.

Should no lesion be found, the mere exploration should result in no serious damage.

After-treatment.—Food should be withheld for thirty-six hours, but a little **water and brandy,** in teaspoonful doses, may be allowed, especially if there is any degree of shock. In that case it is advisable also to use **stimulants** by the rectum or subcutaneously. **Nutritive enemata** of beef-tea and milk are necessary to sustain the patient's powers.

Proctoclysis of normal salt solution according to the Murphy gradual method should be resorted to. The head of the bed should be raised to

apply the Fowler principle favoring the gathering of secretions in the pelvis, where the absorption is less rapid.

> When the patient is placed in the bed [semisitting with pillows under the knees—the Fowler position], quantities of warm **salt solution** are passed slowly into the rectum. The mucous membrane of the large intestine absorbs fluid with great rapidity when that portion of the gut is in its normal condition of moderate distention. Overdistention leads to spasm, which expels the fluid. Hence the fluid must be given at low pressure and administration should be continuous. The simplest sort of apparatus consists of a fountain syringe, a large rubber tube, and a rectal tip of hard rubber. The nozzle that is used is angled, has one opening on the end and several on the side, and this nozzle is passed so that the angle fits to the sphincter. The tube is strapped to the thighs by adhesive plaster. The hose that comes from the nozzle is attached to a reservoir, the base of which is hung from 4 to 6 inches above the level of the patient's buttocks, and the fluid, therefore, enters the rectum only about as fast as the rectum will absorb it. The reservoir is kept hot by bags of hot water. The fluid is allowed to enter continuously, unless it should run out from the side of the tube; if this happens, the flow may be cut off for a short time and then allowed to begin again. Gas from the bowel passes into the openings of the tube, and every now and then bubbles up through the reservoir. By this continuous, low-pressure instillation (protoclysis) an enormous quantity of fluid is absorbed by the rectum. In some cases a number of quarts are taken up in twenty-four hours. The absorption of this fluid greatly increases the amount of urine eliminated and stimulates the heart. The reservoir must not be high. Increase of pressure will cause expulsion of fluid and defeat the possibility of continuous administration. The plan so often followed of keeping the reservoir high and limiting the flow by a clip on the tube is a mistake. Murphy says: "It should never have a headway of more than 15 inches hydrostatic pressure, and it gives the best and most uniform results at 4 to 7 inches" (Jour. Amer. Med. Assoc., April 17, 1909). A straight tube is sometimes responsible for expulsion of the fluid, because it touches the posterior rectal wall of a patient in Fowler's position. J. C. Da Costa (Modern Surgery, p. 1007, 1910).

During this procedure no food should be given by the mouth. If the patient is weak, rectal alimentation is indicated. In the less severe cases liquid food may be permitted by the evening of the second day, and soft, easily digested food after a week, rectal alimentation being continued until then.

The sutures can be removed on the ninth day. The closure of the external wound must be complete before the patient can be allowed to leave his bed, and the danger of a ventral hernia should be counteracted by means of an abdominal supporter.

Hypodermic injections of **strychnine,** $\frac{1}{60}$ to $\frac{1}{30}$ grain, three times a day, according to indications, will prove most effectual in maintaining the strength of the patient and toning the muscular wall of the intestine.

Wounds Due to Military Firearms.

[See *supra,* PENETRATING WOUNDS, for details.]

During the Franco-Prussian War German soldiers were frequently found suffering from wounds of so frightful a nature that the French were accused of using explosive bullets contrary to the International Convention to that effect. Wounded limbs showed lesions of so destructive a character that the hole made

was a *magma* of muscle, tendon, bone, blood, etc. Dead subjects were found with their heads completely shattered, the brains being scattered on all sides. The good faith of the French was soon demonstrated, however, experiments having shown that their rifle, the Chassepot, was capable, when fired at close quarters, of creating unusual lesions on account of the initial velocity and the greater rotation of the bullet. This was attributed mainly to the reduced diameter of the bore, 11 millimeters, and to the increased quantity of powder used.

In 1886 France adopted 8 millimeters as the caliber of her military arm, and the other nations soon followed her example. The United States Government adopted two calibers, one of 7.62 millimeters for the army, and one of 6 millimeters for the navy. Contrary to all expectations, the effects noted in recent wars, the war between Chili and Peru, in which a 7.6-millimeter caliber was used; that between China and Japan, in which a 7.9-millimeter was used on the Japanese side, and the more recent Chitral expeditions and Abyssinian campaigns, in which 7.9-millimeter and 6.5-millimeter arms, respectively, were employed, were less destructive than the larger calibers, while the wounds caused by them healed with greater rapidity than those following lesions due to the action of larger balls. During the Chilian War there were instances where men completely perforated through the chest would suffer from slight shock, a slight hemoptysis, and soon be out.

This radical difference between the destructive power of large and small calibers, or, rather, between the destructive effects of an arm such as the Chassepot (11 millimeters) and the modern rifle (6 to 8 millimeters), is mainly attributed to the fact that lead was formerly employed in the manufacture of bullets; whereas, at present, in order to avoid destruction of the bullet during its progress through the barrel, resulting from the great increase of the powder-charge, and with the view of reducing the weight carried by the soldier, owing to the introduction of repeating arms, the bullet itself is either made of some hard metal, or it is covered with some such substance as nickel, steel, German silver, etc.

These physical features, added to the smaller diameter of the projectile, the much greater velocity with which it travels, its more or less pointed tip, cause it to penetrate soft tissues as would a long, thin blade, separating rather than destroying them. Therefore perforations in a muscle are clean-cut; at times their walls are even collapsed; as a rule, the channel is about the size of the bullet; large blood-vessels are severed and bleed until the heart ceases to beat, etc.

Major Lynch, of the U. S. Army, states that there is considerable difference between the Russian and Japanese rifles. The former has a caliber of 7.6 millimeters; its cartridge weighs 24 grams. The bullet weighs 14 grams and has a jacket of cupronickel. Its initial velocity is 2015 feet per second. The Japanese rifle is 6.50 millimeters in caliber; the cartridge weighs 22 grams; the charge is 2.10 grams of smokeless powder. The bullet, which weighs 11½ grams, is 32 millimeters long and is made of hard lead, with a German silver jacket. The initial

velocity is 2356 feet per second. The different initial velocity, etc., of the Japanese, as compared with the Russion rifle bullet, according to Major Lynch, was not found of great importance, so far as the effects produced by it on the tissues of men hit were concerned, though it is possible that more Russian bullets lodged. The difference in caliber of the two rifles was responsible, however, for very great differences in the wounds caused by them. The wounds due to the Russian bullets were always of a much more severe character. While from the surgical standpoint the extremely small caliber of the Japanese rifle is desirable, it is a great question if they have not carried their desire for long range, flat trajectory, and light weight of cartridge too far, and have thus sacrificed the stopping power of the bullet to such an extent that their weapon does not yield the best results in war. Certainly, a man hit with the Japanese bullet will come on when it has passed through his body anywhere, except at a vital point. The wound of entrance of the Russian bullet was naturally of larger size than that of the Japanese, as was also the wound of exit. The greater destructive effect of the former was, however, most manifest when bone tissue was struck in its course through the body. Bone was almost always extremely comminuted, and the wound of exit caused by the bullet after passage through bone was large. In the winter, at least, many rifle bullets, the Russian more than the Japanese, were deformed by striking hard ground or frozen walls, and wounds produced by such bullets were of course always destructive to both soft and bony tissue on account of the large wounding surface of the missile. Shrapnel bullet wounds were also always of a severe character, both on account of the large size of the shrapnel bullet and because of the material of which it was made—soft lead, which is so liable to deformation. Wounds produced by pieces of shell were even more severe, and frightful injuries were caused by hand grenades. With the last, tissues were so lacerated and torn generally that amputation of injured limbs was almost invariably required. Foreign bodies were not frequently carried into wounds by the Japanese undeformed bullets, and were still more rare with the Russian undeformed bullets. With both deformed they were not uncommon. The shrapnel ball also frequently drove foreign material from the men's clothing into wounds. Fragments of shell sometimes did so, but often tore their way through, carrying everything in their path before them. With hand grenades not only were particles of clothing sometimes carried into wounds by fragments, but stones and dirt were frequently driven in by the explosion.

On the whole, we may conclude that the arms now furnished to armies give rise to injuries far more severe, as a rule, than those met with in civil life, when weapons of various kinds, imparting to bullets a much smaller velocity, are used. Shock is correspondingly more severe, and greater conservatism, in the remedial methods adopted, is necessary.

Treves, Makins and Senn teach that gunshot wounds of the abdomen received in war do better when let alone. In civil life the experience of all surgeons is, that those patients operated

on promptly frequently recover; those treated expectantly usually die. Five personal cases in which recovery followed operation in 4. Holladay (N. Y. Med. Jour., Sept. 26, 1908).

The general aim should be to prevent infection by careful cleansing of exposed tissues, but also to avoid the risk of inflicting additional injury by injudicious instrumental interference and manipulation of the wound.

Though the writer thinks the saying of the English surgeon, that "A soldier shot in the abdomen will live if left alone and will die if operated upon," must be taken *cum grano salis,* he nevertheless pleads for conservative treatment. After abdominal gunshot injury, rest and absolute denial of food and drink is of prime importance. Every soldier should know this. Transportation, if necessary, must be done carefully. Treves reports that all the patients carried from a steep hill with abdominal gunshot injuries died. All patients should be kept at least eight days in the neighborhood of the battlefield. For twenty-four to thirty-six hours the patients receive no food or drink, then teaspoonful doses of water, tea, and gradually milk. No solid food for fourteen days. At first much **morphine** must be used. Persistent vomiting may be alleviated by **lavage,** provided the stomach is not injured. Hildebrandt (Der Militärarzt; Military Surgeon, Mar., 1909).

The value of laparotomy for wounds of the small intestine on the battlefield almost unanimously condemned in general discussion by military surgeons. In the China-Japan, United States-Cuba, Tirah, Transvaal, and Russia-Japan campaigns, operative death was practically universal. This is mainly because facilities are lacking at the front, while the patient is frequently hours on the ground before being operated. Conversely, spontaneous recovery often follows wounds of the intestines by high-velocity and small-caliber bullets. The mucous membrane blocks the opening or muscle-fibers approximate, thus preventing the escape of septic contents. This is soon followed by formation of adhesions. Transactions of the Société de Médecine Militaire (Arch. provinciales de Chir., vol. xviii, p. 267, 1909).

Ernest Laplace,
Philadelphia.

ABORTION.—DEFINITION.—*Abortion* is the expulsion or removal of the fructified ovum before the fetus is viable,—meaning by the term "viable" that the fetus has reached such a stage of development that it can live, thrive and grow, after birth. We cannot say definitely when the fetus reaches that stage, but it has been the custom to consider that it becomes viable at the end of the seventh lunar month or the twenty-eighth week of pregnancy.

Still, a very young fetus may breathe after delivery. This occurred, for example, in 3 cases (2 in the fifteenth and 1 in the nineteenth weeks, respectively) reported by Glöckner. In the first of these there were six respiratory movements before and five after severing the cord, the fetus living one hour. In the second case the fetus lived an hour and a half and breathed five times. The third fetus lived but half an hour and breathed eight times. The autopsy showed air in the stomach, but the lungs were empty.

From a clinical standpoint, however, the fetus is not viable before the end of the seventh calendar month.

[It was hoped by many a few years ago that by means of the modern incubator, and by a special kind of feeding (gavage), fetuses younger than twenty-eight weeks might be raised. The public were much interested. Ingenious mechanics invented many sorts of incubators, some of which were very complicated and very expensive.

These have, in the majority of cases, proved very disappointing. A. H. Wright.]

Premature labor or delivery means the termination of pregnancy between the end of the seventh month and full term. In certain cases it is difficult to distinguish between late abortion and early premature labor.

As to the time of occurrence, it has seemed convenient to consider two varieties: *early abortion,* when it occurs before or about the end of the third month of pregnancy, and *late abortion,* when it occurs between the latter part of the third month and the end of the seventh month of pregnancy.

Three varieties as to the methods of occurrence are also recognized: the *spontaneous,* when the abortion occurs without any outside interference, and is caused by some abnormal condition of the mother or fetus; the *accidental,* when the abortion is due to accident; and the *induced,* when the abortion is produced artificially by interference from outside. Induced abortion is deemed legitimate when it is produced by a physician for just cause. The cause is considered just only when the abortion is induced to save the mother's life which otherwise is imperiled. When the abortion is induced without such just cause, that is, when it is done for improper or immoral reasons, whether by the mother or the professional abortionist, it is known both from a medical and legal standpoint as *criminal abortion.*

The proportion of abortions to labors at term from 1898 to 1904, in six of the Maternity Hospitals of Paris, has risen from about 5.6 to about 16 per cent. More than one-half of these cases are provoked by criminal operations of some kind or other. The proportion of premature labors has also increased considerably. This state of things is due to the tone of modern novels, and to the unhampered propagation of so-called neomalthusian ideas, to books and pamphlets, published and sold broadcast, describing various methods for preventing conception. Doléris (C. r. Soc. obst., gyn., pæd., Feb., 1905).

The number of abortions requiring treatment in the public hospitals of Paris is said to have tripled during the last few years; Treub estimates the criminal abortions as 10 per cent. of all observed in Amsterdam, and others there estimate the proportion up to 33 per cent.; at Utrecht, nearly 14 per cent.; at Groningen, 24 per cent., and the author cites several American authorities and others to show the increasing importance of this subject. Warning against making a local examination of a woman threatened with abortion. If absolutely compelled to make an examination, the finger should never be introduced until after the external genitals have been prepared as for a vaginal hysterectomy; otherwise, puerperal infection is likely to ensue sooner or later and the physician alone will be responsible for it. De Bovis (Semaine médicale, Oct. 26, 1910).

Three cases of fatal mercurial poisoning from bichloride tablets used to produce abortion. In one of these the young woman introduced into the vagina to produce abortion 6 bichloride tablets, each containing 7.3 grains. This produced severe and burning pain and such muscular spasm that the patient could not remove them. A physician was promptly summoned, who gave vaginal douches of warm water and morphine hypodermically. The patient speedily developed intense symptoms of mercurial poisoning, and died four days later. At autopsy an intense necrotic exfoliative enterocolitis was present, most severe in the rectum. The process was distinct as high as the duodenum. There was also necrosis of the muscular walls of the vagina and vaginal portion of the cervix. The broad ligaments, Fallopian tubes, and ovaries were necrotic, but above the internal os the lining of the uterus was

normal. There was no evidence of peritonitis. Schildecker (Amer. Jour. of Obstet., March, 1911).

As to frequency, it is impossible to estimate even approximately the proportion of pregnancies terminating in spontaneous abortions. Women who object to having large families have such a multitude of expedients to cut short their pregnancies, and frequently conceal their methods so carefully, that our estimates as to percentages cannot be exact. From the results of our experience in private practice it is indicated that abortion occurs from accident or spontaneously in 1 out of 10 pregnancies, that is, 10 per cent. However, if we include induced abortions (legitimate and criminal), it is probable that abortion occurs in 3 out of 10 pregnancies, that is, in 30 per cent.

The figures of the Paris Maternité from 1897 to 1905, as collected by G. Rimette, show 9875 pregnancies, 1457 abortions, 627 spontaneous abortions, 414 complicated abortions, 367 infected abortions, and 27 deaths from abortion.

Michailoff, who bases his figures on 257,988 births in one of the Russian maternities, found that the proportion of abortions to full-term deliveries was about 1 to 10. Keyssner, in his polyclinic material, found 469 abortions to 2623 confinements, or 1 to 5.6. The figures of hospitals are bound to be faulty, since they omit the numerous cases that are taken care of at home. Even polyclinics, where the physician attends the patients at their home, do not give an accurate idea as to frequency, for many mothers have an abortion with hardly an untoward symptom and absolutely without medical attention.

As Chazan points out, the only accurate statistics are those obtained through the patient's anamnesis. The evidence thus far at hand from such sources is very insufficient. For this reason the author undertook the labor of looking over the clinical records of 600 patients treated at the gynecological clinic of the Washington University Hospital. He found that 348 out of these 600 women had been pregnant. Of this number there were 870 full-term pregnancies by 293 mothers, 371 abortions by 201 mothers, 36 confessedly criminal abortions, 50 women who developed some gynecologic disease after abortion. *This would make the ratio of abortions to confinements, 1 to 2.3.* This means that every third pregnancy does not develop to viability, a loss to the world of one-third of all the children that are conceived. F. J. Taussig (Amer. Jour. of Obstet., Oct., 1908).

Miscarriage.—We consider abortion and miscarriage are synonymous terms. In former times the terms were not considered so, nor are they now in some quarters. Many, if not all, of the Rotunda men, and some obstetricians of North America, still use the term miscarriage in the old-fashioned way. According to them, miscarriage is a term applied to the expulsion of the ovum between the beginning of the fourth and the end of the seventh month, that is, between the time of the complete formation of the placenta and the time that the fetus becomes viable. Those who thus define miscarriage say that abortion is the term applied to the expulsion of the ovum before the end of the third month, that is, before the complete formation of the placenta.

[It should be remembered that a large proportion of the laity think that abortion is the term used when the uterus has been emptied by artificial interference. It is well, therefore, for the physician when speaking to his patients to use the term miscarriage. Some women are offended if the physician hints at the possibility of their having had an abortion. A. H. Wright.]

SYMPTOMS.—The symptoms of abortion are hemorrhage, a brown

discharge after the death of the ovum, pains in the pelvis, complete or partial dilatation of the os uteri, expulsion of the whole or part of the ovum.

The hemorrhage in the majority of abortions is not profuse, and may continue a long time. In a certain class of cases, however, the hemorrhage is very profuse and sometimes causes death. Some think that hemorrhage in early abortion is never profuse enough to cause death. Certainly the hemorrhage before the formation of the placenta is seldom dangerous to life. There are exceptions to this rule, however; but, so far as we know, the majority of the fatalities from hemorrhage in early abortion occur in cases of criminal abortion where sharp or pointed instruments are used.

> Case of fatal hemorrhage in a multipara of 44 years, four months pregnant. The hemorrhages had recurred daily for eight weeks, but were severe only during the last two weeks, causing marked anemia and exhaustion. The uterus was emptied under anesthesia after dilatation of the uterus, but this was followed by bleeding which hot irrigation, saline solution, massage, or tamponing failed to control. The uterus was then removed through the vagina in nine minutes, but, although no blood was lost, the patient gradually sank. Careful macroscopic and microscopic examination of the organ failed to reveal any morbid condition of any kind. Henze (Zentralbl. für Gynäk., Nu. 29, 1908).

In considering the symptomatology of abortion, however, it is very important to obtain a clear conception of the two varieties commonly recognized, viz.: the "threatened" and the "inevitable."

[The importance of this distinction asserts itself in connection with treatment. In the case of threatened abortion we are in doubt as to whether the uterus will be emptied or not, and our treatment aims at controlling the influences which are producing the symptoms of abortion, such as hemorrhage and uterine contractions. In the case of inevitable abortion the contents of the uterus will be held or partially expelled by nature's efforts, and we pursue a line of treatment entirely different from that adopted for threatened abortion. Our aim now is to assist nature in expelling the contents of the uterus as soon as possible with safety to the mother. A. H. Wright.]

The symptoms of *threatened abortion* are hemorrhage, pelvic pain and perhaps a slight dilatation of the os, especially in multiparæ. The hemorrhage, as already mentioned, is comparatively slight in a large proportion of cases, and may continue for nine or ten weeks or longer without ending in actual abortion. The pains which are caused by uterine contractions may be fairly severe and may continue for some time without causing the expulsion of the ovum.

> External hemorrhage is not only the most important, but the most common premonitory symptom of abortion, and although it may be induced, atony of the uterus is its most frequent cause. Under such circumstances it may appear as early as the sixth week of pregnancy, about the time when the serotinal vessels begin to undergo rapid enlargement in response to the stimulation of the placental chorion. Hemorrhage may also be due to deficiency of calcium and potassium in the muscular substance of the uterus, or to the presence of some toxic material impairing the tone and responsive power of the organ. In such cases potassium iodide and calcium chloride are given to remove deleterious substances or to supply those which are deficient. When the muscular energy of the uterus is impaired there is often enfeeblement of the nerve energy also, and strychnine, arsenic, digitalis, or phosphorus may be given with benefit. Pain is the other all-important prodromal symptom of abortion. It may be

noted when the uterus does not adequately respond to and fails to expand correlatively with the developing ovum. The uterine tissues, again, may be responsive enough, but they may be restrained by adhesions. Abortion not infrequently results from physical or mental shock, or a combination of both influences. After the tenth or twelfth week of pregnancy the uterus may be injured directly by a blow on the lower abdomen, and abortion may more or less quickly ensue. But usually there is extravasation of blood from rupture of the functionally active maternal vessels; the blood may never make its escape externally, and pain may be the only symptom. No drugs should be given in such cases; absolute rest is the best treatment. Necrosis of the amniochorion is a very rare cause of abortion, and it determines this event by allowing the amniotic fluid to escape. J. Oliver (Brit. Med. Jour., Nov. 30, 1907).

In inevitable abortion there are also hemorrhage, pelvic pains and more or less dilatation of the os, but these phenomena are more severe and pronounced. It is sometimes, in fact, very difficult to decide when an abortion becomes inevitable. Probably the safest guide is the hemorrhage. If the fetus is dead, or if the membranes are ruptured, abortion is also deemed inevitable. No definite rules can be given in this regard.

That abortion is inevitable when the membranes are ruptured is generally believed to be true in every case, but 3 personal cases have proven to be exceptions. In the first, a young woman in her first pregnancy, a fall caused rupture of the membranes at about the end of the sixth month; a large quantity of amniotic fluid escaped, and pains came on with some dilatation of the os. With rest in bed and a free use of viburnum the patient recovered and went on to end of seventh month, when there were pains again; the same treatment was followed by the same result, and the writer delivered her at full time of a healthy boy. In the second case the membranes ruptured during the eighth month, but was not delivered until the end of the full term of a living, healthy boy. In the third case the membranes had ruptured three weeks before the present writing and had not delivered yet. J. R. N. Smith (Communication to the Editor, 1908).

[This communication is interesting, but the writer furnishes no evidence to show that the discharge of the fluid in any of the 3 cases was due to rupture of the membranes. It seems probable that the discharge of watery fluid in each instance was due to that mysterious condition the nature of which we know but little about—hydrorrhœa gravidarum, or decidual endometritis. A. H. Wright.]

The symptomatology of abortion varies, of course, to a certain extent according to the time at which it occurs. As carefully collated by Lutaud, of Paris, the symptoms at the different periods are briefly as follows:—

Abortion During the First Month.—This usually gives rise to symptoms simulating those of retarded menstruation. Slight pains in the back in the region of the uterus are complained of; the symptoms, in this particular, resemble those of normal labor, but are very much less marked. Blood, blood-clots, and flakes of the mucous membrane of the uterus are gradually expelled during several days. The ovum is expelled entire, but it is so small that it is rarely discovered.

Abortion During the Second Month.—Inasmuch as the uterus has decidedly increased in size as compared with its size in the first month, the contractions and pains are comparatively stronger. The embro is usually expelled inclosed in the unbroken

membranes. Sometimes, however, the latter are ruptured.

The embryo and membranes may be detached from the uterus in two ways:—

(*a*) By hemorrhage between the membranes and the uterus, followed by uterine contraction.

(*b*) By contraction of the uterus, followed by hemorrhage. In the latter case the abortion is more prolonged, the membranes being detached but slowly from the uterus.

If the embryo be still living, the abortion lasts longer, and the hemorrhage is greater. If the embryo be dead, the whole is usually expelled like a foreign body, and without rupture of the membranes.

Examination of the uterus will show that it is increased in volume and situated lower down in the pelvis than normally. The cervix is dilated, softened, and filled with blood-clots. The dilatation is more marked in multiparæ than in primiparæ.

The cervix, though dilated, does not become effaced, and the embryo contained in the unruptured membranes may pass through the cervix and be expelled. If the membranes are ruptured, however, the embryo passes by itself, the very thin umbilical cord breaks, and the cervix closes. The membranes are, in this latter case, expelled later on. The membranes are ruptured about once in every 2 cases.

Abortion from the Beginning of the Third to the End of the Fourth Month.—This occurs nearly always in two stages, the first consisting in the expulsion of the fetus, and the second in the expulsion of the membranes and placenta.

The cervix in this form of abortion tends to diminish in length. The uterine contractions act more powerfully than in the previous forms of abortion. Under their influence the membranes are ruptured and the fetus is expelled.

The placenta may still be adherent; the cervix then closes again, and the placenta and membranes are expelled later on. Hemorrhage is likely to accompany the delivery of the placenta and membranes, especially when the former is only partly detached. Under these circumstances each uterine contraction is accompanied by hemorrhage.

The placenta may be already detached when the fetus is expelled; in such a case it is likely to be expelled immediately after the latter, before the cervix closes, but part of the decidua may remain in the uterus after delivery of the placenta. This occurs most frequently when the fetus is dead.

Statistics show that retention of the placenta occurs most frequently during this period.

Abortion During the Fifth and Sixth Months.—The fetus and placenta are almost always expelled separately. Uterine contraction is more marked; the cervix tends to become more effaced and to dilate.

Delivery of the placenta usually follows delivery of the fetus rapidly, and the tendency to hemorrhage is less marked than in the previous forms of abortion.

Of 501 cases of abortion analyzed by Varnier and Brion, the fetus, or embryo, and the placenta were expelled separately in 453, and together in 48 cases. When the delivery occurred in two stages, the time found to elapse between the expulsion of the

fetus and that of the placenta was as follows: 120 cases, within 15 minutes; 81 cases, from 15 to 30 minutes; 78 cases, from 30 to 60 minutes; 83 cases, from 1 to 4 hours.

Whenever the placenta and membranes are not expelled within four hours after the expulsion of the fetus, or embryo, there is retention of the membranes and placenta.

Abortion may take place suddenly, or resemble, in that particular, the irregular periodicity of normal labor, with more or less hemorrhage. It may, indeed, last several days, owing to weakness of the uterine contractions or adhesions to the uterus or retention in the cervix of the masses to be expelled. (Rokitansky, Schülein.)

Sudden or rapid abortion is frequent during the first two months; when the expulsion takes place after the third month it generally presents the characters of normal delivery.

The menstruation returns earlier after abortion than after a normal labor. Engländer, in a recent (1906) study of 57 cases of abortion, undertaken to ascertain the period of their first subsequent menstruation, found that in 64.9 per cent. the menses reappeared in four weeks; in five weeks in 14 per cent. The remainder varied, 1 patient going as long as six weeks after the abortion before menstruating. After labor, it is usually six to eight weeks before patients menstruate.

DANGERS.—Just as parturition may be attended by deviations from the normal, so may abortion.

Retention of the placenta occurs frequently. The latter is sometimes expelled safely after some days, either entire or in pieces, but prolonged retention exposes the patient to hemorrhage, toxemia, and septicemia. When completely detached, though retained, the placenta gives rise to no hemorrhage, but if only partially detached such is not the case and copious hemorrhage may thus be produced.

> In 15,000 cases of abortion, fever occurred in 15 per cent. Of 633 patients, 182 had chills before they came under active treatment. Among the 15,000 patients were 450 who were severely infected; of these 94 died. In 82 cases autopsy was made. Those cases showed the most severe symptoms in which the longest time elapsed before the uterus was completely emptied. Fever often ceased when the uterine contents were expelled. These were cases of pure sapremia in which the bacilli present were only mildly infective. It is of the utmost importance that no artificial wound be made in the lining membrane of the uterus. In these cases neither incision nor forcible dilatation should be practised, but if necessary the cervix should be tamponed with gauze until the uterus is sufficiently open to permit the removal of its contents with the finger. No sharp instrument should be employed in the treatment of abortion. Seegert (Zeit. f. Geb. u. Gyn., Bd. lvii, H. 3, 1906).

The general symptoms that follow hemorrhage (a weak pulse, vertigo, fainting, etc.) occur only when the loss of blood has been severe. Under these conditions septicemia, as evidenced by fetid lochia, chills, and high temperature, is a probable complication. Endometritis, salpingitis, and peritonitis have also been witnessed under such conditions. Tetanus is also another possible complication of these cases.

> Case of tetanus after abortion. The latter occurred during the third month. The uterus was properly cleared, but on the ninth day the temperature rose, then fell after an injection of collargolin. Trismus was observed on the next day, followed by tetanus, which grew

worse till the fifteenth day. Numerous injections of Behring's tetanus antitoxin were administered, and recovery followed. Osterloh (Monats. f. Geb. u. Gyn., Aug., 1902).

ETIOLOGY AND PATHOGENESIS.—There has been much theorizing as to the causes of abortion, and in many instances, the explanations and complicated classifications vouchsafed have obscured the subject instead of elucidating it.

The causes of abortion are usually considered in an unsystematic and illogical way. We should differentiate between conditions of the uterus which predispose to expulsion of the ovum and conditions which excite the uterus to get rid of its contents. The predisposing causes are: 1. Increased sensitiveness to nerve irritation (temperament, frequent abortions, menstrual period). 2. Greater tendency to placental thrombosis (inflammation of endometrium, congestion). 3. Lessened resistance to expulsion (cervical tears or amputation).

The exciting causes are: 1. *Mechanical Irritation:* (*a*) transmitted (blow, fall, dancing, railroad journey, lifting heavy objects, constipation); (*b*) direct, (1) to outside of uterus (adhesions, malposition, tumors, examination, laparotomy); (2) to inside of uterus (instruments, hemorrhagic exudates, hydramnios, tumors).

2. *Thermic Irritation:* (*a*) general (sea-bath); (*b*) local (hot douche, sitz-bath).

3. *Toxic Irritation:* (*a*) chemical toxins (ergot, carbon dioxide, lead poisoning); (*b*) bacterial toxins (maternal small-pox, measles, etc.); (*c*) placental toxins, hyperemesis, chorea, eclampsia.

4. *Nerve Irritation:* (*a*) psychic (fright, pain, shock); (*b*) reflex (external genitals, breast, nose).

5. *Death of Fetus:* (*a*) congenital inanition (illness of parents, alcoholism, too frequent coitus); (*b*) congenital deformities (primary in ovum, amniotic adhesions); (*c*) interference with nutrition: (1) maternal (anemia, tuberculosis); (2) placental (mole degeneration, thrombosis); (3) umbilical (twisted cord, true knot, constrictions); (*d*) infectious diseases (syphilis, small-pox, typhoid, pneumonia, etc.); (*e*) hyperpyrexia. Taussig (Amer. Jour. of Obstet., Oct., 1908).

Series of cases from Aschoff's institute in Freiburg in which specimens of Fallopian tubes removed after cases of abortion were examined It was found that after a normal pregnancy in labor there was no inflammatory reaction in the Fallopian tubes, but that after dilatation of the cervix with laminary tents, although careful asepsis had been employed in a large majority of cases, there was an inflammation of the tube which had gone on to purulent salpingitis and lymphangitis. This pathological observation is increased evidence of the difficulty of conducting vaginal operations aseptically. Amersbach (Monatssch. für Geburts. u. Gynäk., Bd. xxxii, Hft. 4, 1910).

It is generally recognized, however, that the causes may be of maternal, paternal, and fetal origin.

Maternal Causes.—Most cases of abortion are generally attributed to traumatisms, falls, blows—a cause not infrequently met with in the slums—the likelihood of premature delivery being decreased in proportion as the blow or other injury is remote from the region of the uterus. Operations, even sometimes when insignificant, have produced abortion. The so-called "aborting habit" is also recognized as a potent factor in this connection; but this expression doubtless covers, in most instances, some hidden and probably removable cause.

In most cases the actual cause of a miscarriage escapes observation. Commonly it is attributed to a vague traumatism; often to a fall on the stairs. In reality the pathogeny of abortion is as follows: The ovum plays the part of a foreign body and is expelled, first,

when it is itself changed by death, separation, or other cause, though contained in a normal uterus; second, when, whether healthy or not, it is contained in an intolerant uterus. The causes which may produce these conditions are changes in the ovum, pathological conditions in the uterus, faults in the general health of the woman, and vitiation of the spermatozoa. Traumatism varies greatly in its power to interrupt pregnancy according to its intensity, the seat of its application, its severity and repetition, the age of the fetus, and the degree of the idiosyncratic irritability of the uterus. Bonnaire (Presse médical, May 3, 1905).

The predominating cause, however, according to statistics, is syphilis, to which are attributed over one-fourth of the cases. When it is contracted before conception, abortion occurs repeatedly—early when the infection is of recent date, but gradually nearer term as the contamination is more remote. There comes a time, therefore, when normal delivery becomes possible.

Next in order are malpositions and inflammatory disorders and tumors of the uterus and its adnexa, including ovarian cysts. Laceration of the cervix has recently attracted attention as a cause of abortion. The tear may be limited to the cervix, or it may extend upward to the body of the organ; or again the rupture may occur above the external os.

Charpentier refers to three distinct local uterine conditions in otherwise healthy women: 1. Ill-developed uterus; the muscular coat does not readily soften, yet remains very irritable. Rare. 2. Displacements, especially flexions. Spur at the angle of flexion hypertrophies interferes with uterine development. 3. Congestion of the body and cervix, due to idiosyncrasies. Endometritis.

Lacerations of the cervix, especially those of some depth, are a frequent cause of abortion. A primipara can usually give some cause for an abortion, such as a misstep or a fall, but in those who have previously borne children, where there is a fissure extending as high as the internal os that will admit the tip of the index finger, or the integrity of the lower uterine segments is lost, predisposition to abortion is undoubted. R. W. Rogers (Montreal Med. Jour., April, 1902).

One of the rarer causes of abortion is laceration of the cervix; but if the laceration is repaired a subsequent pregnancy will often proceed to term, as the writer has seen happen twice in 11 cases. Among other causes of habitual abortion not generally known are residues of past inflammation of the pelvic peritoneum, three or four instances of which he has met with. Sterility is usually associated with exudations in the parametrium, and even should conception occur the pregnancy seldom persists to term. The writer has also seen abortion due to fibroma of the uterus, four times; to heart disease, three times; to diabetes mellitus, twice; to hydramnios in two instances, and to pulmonary emphysema in one. Kleinwaechter (Zeit. f. Geb. u. Gyn., Bd. xlix, H. i, 1903).

Case of a primigravida, in whom it was necessary to terminate an early pregnancy. Iodoform gauze was introduced into the cervix, followed by the development of considerable pain. The temperature rose also; the pulse increased in frequency; the uterus became very sensitive, and there was a fetid mucous discharge. To hasten the emptying of the uterus, tents and bougies were used. This was followed by increase in pain. Twenty-four hours afterward examination showed that the cervix had not dilated, but had ruptured above the external os. It was necessary to empty the uterus completely under anesthesia and to remove portions of the cervix which had already been torn. The patient recovered, the tears healing by granulation. Blumreich (Zentralbl. f. Gyn., Nu. 29, 1907).

Debilitating influences of various kinds, such as insufficient food, excessive physical labor or fatigue, mental and physical shock, the abuse of alcohol, tobacco (women employed in cigar, cigarette, etc., factories), carbonic oxide (as shown by the frequent occurrence of abortion in cooks) and lead, including paternal intoxication by this metal, tend also to bring on miscarriage.

> In south Yorkshire 10 out of 18 women who suffered from lead poisoning admitted that they had used lead as an abortifacient. In 11 of the cases abortion had actually occurred. The fact is important, and shows that lead poisoning must be kept in mind when such symptoms as abdominal pain, vomiting, and constipation are present in women who are supposed to be pregnant. Thomson and Littlejohn (Edinburgh Med. Jour., June, 1905).

> Great shock or injury is sometimes better borne by pregnant women than frequently repeated shock, *e.g.*, the use of the sewing machine with the foot. The author reports cases illustrating the fact that motoring during the early months of pregnancy is frequently followed by abortion. The danger seems to lie in the fact that the rapid motion of a motor car subjects the patient to many small, frequent jars. The characteristic of abortion following motoring is its slow and insidious development without bright hemorrhage or pain. These abortions are, as a rule, incomplete, and require curetting. While motoring is dangerous in early pregnancy, in the later months of gestation and with reasonable precautions as to smoothness of roads and moderation of speed it may prove exceedingly useful. Davis (Medical Record, Jan. 30, 1909).

Debilitating diseases have also been found to induce it. Influenza, in which the general adynamia is marked, has been recorded as a cause. In Asiatic cholera, abortion is almost invariably produced.

Conversely, conditions which tend to exaggerate the contractility of the uterine muscle are also recognized causes. Ergot, copper sulphate and other "abortifacients" are familiar agents of this class. This evil action has also been attributed to quinine, but there is reason to believe that this valuable remedy should not be withheld in pregnant women, when indicated therapeutically, especially in view of the fact that malaria itself tends to cause abortion. Thus, in a study of the action of quinine on pregnant women, Frederici found that in 49 pregnancies quinine had been used in 47, the patients suffering more or less severely from malarial fever; 47 terminated at the usual period by the birth of a child, and 2 aborted. In these 2 cases he deems it extremely probable that the high fever from which they suffered was instrumental in producing abortion. He concluded that medicinal doses of quinine were powerless to induce abortion.

> Case of a hospital nurse, pregnant two months, who attempted to induce abortion by injecting into the uterus 1 gram of Fehling's solution. She reported her act within half an hour. The symptoms she then presented were extreme anxiety, coolness of the skin, and decided slowness of the pulse. There was no bleeding. The following day the pulse had become improved, there was considerable vomiting, and the urine was extremely dark. The urine gradually became bloody, and at the end of five days showed many casts. All the toxic symptoms gradually disappeared, but no abortion took place. Tantzscher (Zentralbl. f. innere Med., Jan. 5, 1907).

Infectious diseases provoke abortion in a large proportion of cases when the febrile period is reached. It occurs in about two-thirds of preg-

nant women attacked by typhoid fever, especially during the earlier months. Uterine hemorrhage is usually the first symptom observed. Thus Sacquin collected 310 cases, and found abortion in 199; while Martinet found 66 abortions in 109 cases.

Small-pox causes abortion in about 40 per cent. of the pregnant women it attacks and the mortality is about 50 per cent., but is nearly 100 per cent. in the confluent type. In varioloid the child sometimes remains unaffected. The disease may also develop during convalescence. Abortion during variola is apt to be attended with more than the ordinary hemorrhage.

Arnaud has reported several serious cases occurring during convalescence after small-pox. The grave symptoms are attributed to the retention of the fetus, which died during the acute stage of small-pox, and was frequently only expelled during or after convalescence.

Measles is an infrequent complication of pregnancy, but, as observed by Klotz, it causes abortion in the majority of such instances. Pneumonia frequently appears as an additional complication. Scarlatina is also infrequently observed in pregnant women, though it is commonly observed during the parturient state.

Pneumonia causes abortion in about one-third of the pregnant women it attacks early and in two-thirds of those which contract the disease late. In the latter cases the fetus, though viable when born, may soon die of the infection after birth. The statistics of 213 cases of pneumonia during pregnancy published by Flatté showed that the pregnancy was interrupted in 118 cases, there being 42 abortions and 76 premature deliveries. Death of the mother occurred in 75 cases among the 213: a mortality of 35 per cent. The mortality of the mother was greater in premature deliveries than in abortion.

Pulmonary tuberculosis, owing to its exhausting influence upon the nutritional resources of the body, renders it unfit to carry the fetus to term when the morbid process is far advanced. Abortion is relatively frequent in such cases, its occurrence and the viability of the child depending upon the stage of the disease.

Chorea, though a rare complication of pregnancy, causes abortion in one-half of the cases, and is especially observed in primiparæ. If the delivery occurs sufficiently late, the child may live, but is frequently affected with chorea. The chorea sometimes ceases after delivery.

Cardiac diseases influence pregnancy when it is sufficiently marked to impair the general circulation. Acute pericarditis practically has no morbid influence on gestation, but chronic pericarditis is deemed pernicious. Acute endocarditis assumes increased virulence during pregnancy, its tendency being to become ulcerative, and to entail a fatal ending.

Icterus, in its various forms, sometimes complicates pregnancy. Even simple catarrhal icterus may cause abortion, but in icterus gravis it occurs always and usually proves fatal. In the epidemic icterus of pregnancy, the probability that abortion will occur is somewhat smaller, while the mortality is not as great. Pregnancy not only aggravates even simple icterus, but it increases the tendency to yellow atrophy of the liver.

Paternal and Fetal Causes.—The influence of syphilis on abortion has

been reviewed; in most instances it is acquired from the male directly, either before or after conception, the disease being communicated to the fetus, in the latter case, through the placenta. In accord with Colles's law, the fetus may, as is well known, inherit the paternal syphilis, while the mother remains immune. Abortion may thus be caused through maternal or fetal syphilis acquired from the father.

Any condition such as senility, alcoholism, overwork, etc., which tends to lower the vitality of the father tends also to weaken the offspring and promote the tendency to miscarriage in the mother. Certain occupations which expose the patient to the action of certain poisons, mercury, phosphorus, or lead, for instance, tend in the same direction.

Besides the features which tend to compromise the development of the fetus that have been referred to, it is itself subject to injuries communicated from the exterior, blows, shocks, penetrating wounds (knife, bullets, etc.), etc. The application of X-rays has recently been added to the list of known causes.

Experiments on guinea-pigs which fully confirm those of Tellner, showing that even short exposures of the abdomen to the action of the rays is liable to destroy the life of a fetus even shortly before term. Alterations were found in the ovaries suggesting sterility. The cause of the fetal death could not be determined macroscopically. Lengfellner (Münch. med. Woch., Nu. 44, 1906).

Case of a tuberculous patient in whom it was determined to interrupt pregnancy with the hope of checking the tuberculous process. Twenty-five applications of the Röntgen rays were made, each lasting from five to ten minutes. After each five days a pause of one day was allowed to intervene before new applications were made. The regions over the ovaries and the thyroid gland were chosen for the applications. Especial care was used to avoid injury to the skin. Spontaneous abortion occurred with free hemorrhage, which ceased when the uterine contents were expelled. No vaginal examination was made during the case, so that the effect is attributable entirely to the Röntgen rays. Fraenkel (Zentralbl. f. Gyn., Nu. 31, 1907).

Low or vicious attachment of the placenta, degeneration of the chronic villosities, hydramnios are the remaining main abnormalities which affect directly the fetus and cause its premature elimination by the uterus.

PROGNOSIS.—Considerable loss of blood may occur in a case of threatened abortion, and yet the patient, when properly treated, proceeds to full term. Cases of spontaneous abortion unattended by complications practically always recover. The degree of antisepsis has much to do with the result however; while, for example, in Pinard's service where rigorous asepsis was observed the mortality was only 0.81 per cent.; corresponding cases (which included favorable and unfavorable) outside his services reached 27.5 per cent.

Six hundred and ten cases treated at the Boston City Hospital (1892-1902); 29 deaths, or 4.75 per cent. They included a large proportion of induced and neglected cases. The deaths include cases with pre-existing typhoid and pneumonia. With two exceptions those of the 29 deaths obviously due to the miscarriage were caused by septic pneumonia following a miscarriage between four and six months. The other 2 were due to sepsis after abortion at the third month.

There were 418 cases treated as outpatients of the Boston Lying-in Hospital (1892-1902). There were 5 deaths, or 1.2 per cent.; 1 case could not be

traced. The 5 deaths were due to (1) typhoid; (2) pyonephrosis; (3) pulmonary embolism; (4 and 5) sepsis. Of the 1028 cases but 7 were twin pregnancies. Friedman (Boston Med. and Surg. Jour., Nov. 20, 1902).

TREATMENT. — Treatment of Threatened Abortion. — When the symptoms of threatened abortion appear we should endeavor to stop the morbid process, especially when the hemorrhage is not copious, the pains are not severe, and there is no evidence of the escape of liquor amnii. Our chief aim should be to keep the patient absolutely quiet, by ordering her to bed, and relieve the pains due to uterine contractions by means of opiates in suitable doses. **Opium** seems to be better than morphine, even when the latter is given hypodermically. The tincture of opium, 30 minims (2 Gm.) should be given by the mouth, followed by 15 minims (1 Gm.) every hour, repeated three or four times if required. Or, better still, 2 grs. (0.13 Gm.) of the aqueous extract of opium can be given as a rectal suppository, and 1 gr. (0.065 Gm.) every hour afterward, three or four times if needed. If **morphine** be preferred, ½ gr. (0.032 Gm.) may be given hypodermically, and ¼ gr. (0.016 Gm.) every hour, therefore, for three or four doses if required. An excellent plan when one wishes speedy effect from the opiate is to give at once ½ gr. (0.032 Gm.) morphine hypodermically, and 15 minims (0.92 Gm.) of tincture of opium by the mouth every hour afterward, or 1 gr. (0.065 Gm.) of **extract of opium** in a suppository every hour afterward for three or four doses if required.

[Some physicians will consider that such dosage is large. Many physicians and obstetricians grew timid about the use of opium because of the violent antiopium riots that broke out in many surgical camps about twenty years ago, after Lawson Tait told the abdominal surgeons of the world that opium was an abomination which must be discarded in their work forevermore. The pendulum has turned, however, and is going the other way. A. H. Wright.]

We ought, of course, to consider that opium should be given with great care. At the same time, the writer thinks it absurd to give, for instance, 10 minims (0.61 Gm.) of tincture of opium by the mouth, three times a day, for the pains of threatened abortion. As a rule such doses will have no good effect, because they will not relieve the pains, and they may have a bad effect by causing constipation. Opium does cause constipation, and thus interferes with elimination, but the writer does not admit that it causes complete paresis of the intestines. Sepsis alone causes that kind of paresis.

The constipation caused by opium can be easily overcome by the administration of ordinary **laxatives.** If, however, the physician who has given opium in the case of threatened abortion is afraid to use mild cathartics for constipation, he might order an ordinary **enema.**

Some years ago the administration of **viburnum prunifolium** was supposed to have a good effect in cases of threatened abortion. The result of recent experience does not indicate that such supposition is correct. The writer considers it practically worthless. The fluidextract, ½ to 1 dram every three hours, or 10 drops every hour, with **chloral hydrate** 8 grains, have, however, been found effective in arresting uterine contractions when opium could not be used or when its constipating effects might prove

detrimental. Or, **chloral hydrate**, 10 grains, and **potassium bromide**, 20 grains every two or three hours, may be preferable, since the hypnotic tends to insure the absolute rest and quiet that should be observed to obtain a satisfactory result. **Codeine** is preferred to other opiates by some obstetricians.

Treatment of Inevitable Abortion.—There never has been, and probably never will be, a consensus of opinion among obstetricians as to the treatment of abortion. It seems convenient to consider that there are three general plans: expectant treatment, treatment by tamponade, forced dilatation of the cervix and curettement.

Expectant Plan.—The term expectant is not a good one as a rule, and it becomes most unsuitable if it is misunderstood.

[A prominent gynecologist once wrote: "In my early experience, cases of abortion were treated by the so-called expectant plan, a wretched makeshift, and one that should never be entertained. This plan consists of daily visits by the doctor, who trusts entirely to Dame Nature without giving her any assistance. When fever sets in it is looked upon as a calamity that could not be avoided. The mother dies from what is called a bad hemorrhage, and a life is lost that should have been saved." It is possible that grossly incompetent practitioners allow their patients thus to die without giving any assistance, but we have never seen anything of the sort. We wish to state positively that the above description of expectant treatment is incorrect. No good obstetrician has ever advocated anything so absurd as this sort of *do nothing* treatment. A. H. WRIGHT.]

Lusk was perhaps the most prominent advocate of the expectant plan of treatment. He urged that, when in the third month the ovum is thrown off without the rupture of the membranes, the hemorrhage rarely assumes dangerous proportions, and explained how the uterine contractions sometimes pressed the ovum into the cervix. During these uterine contractions the ovum descends and the upper portion of the body of the uterus retracts. Some coagulation of the blood takes place between the ovum and the retracted uterine walls, while the ovum forms a tampon which fills the cervix like a ball valve, and thus restrains the hemorrhage. When there is no interference, the ovum, after being retained for a time

Ovum, five weeks.

as described, is frequently expelled entire, leaving the uterus in the best possible condition for satisfactory involution. In such cases, and they are by no means uncommon, nature has done well. Why should we try to improve or interfere with such magnificent work?

Removal of the Uterine Contents.—It should be definitely understood that, while nature is doing good work, we should watch carefully, and be ready to assist when her efforts have ceased to be efficacious. When the os and cervical canal are sufficiently dilated to allow the introduction of the finger into the uterine cavity, and the uterine

contents are not extruded, we should interfere, and endeavor to empty the uterus. We should presume, unless there is positive proof to the contrary, that the ovum is intact, and should not be broken.

The author epitomizes the consensus of opinion in regard to the indications for therapeutic abortion. Should therapeutic abortion be used to save a function or a sense? Germann has made a thorough study of the eye troubles incident to pregnancy, and concludes that eye complications dangerous to sight, such as ulcerative keratitis, justify the termination of pregnancy with the object of saving as much sight as possible to the mother. The several forms of autointoxication frequently produce eye diseases which justify abortion. Shall therapeutic abortion be resorted to to save the life of the mother when the termination of that life seems otherwise inevitable? Today, when the maternal mortality from Cæsarean section in elective and uninfected cases is practically *nil,* the physician has no right to sacrifice the fetus, since he has this method of delivery at command.

In hyperemesis, or incoercible vomiting of pregnancy, which occurs once in about 1000 pregnancies, the mortality is about 50 per cent. under treatment by drugs alone. The question as to when abortion should be induced to save the patient's life has been satisfactorily answered by Norris, who, after painting a graphic picture of the earlier stage of this condition, and describing the final stage when the "typhoid" state appears, with rapid, feeble pulse, weakened heart-sounds, fever, restlessness, diminished urine with albumin and casts, and finally delirium, stupor, coma and death, observes that "induction of abortion, to avail, must not be delayed until this typhoid condition appears; it must be resorted to in the earlier stage."

In tuberculosis, artificial termination of pregnancy promises good results only when practised in the early months. Rosthorn favors induction of abortion in tuberculous processes, whether new or old, while Kuttner says that without interruption of pregnancy the prognosis in tuberculosis of the larynx is exceedingly unfavorable for both mother and child. Many authorities might be cited to show that the interruption of pregnancy had been followed by marked improvement in the patient.

Chronic nephritis is often an indication for therapeutic abortion, and among others which have been deemed justifiable indications may be mentioned mitral or aortic lesions, pyelitis and pyelonephritis, advanced diabetes, hydramnios when associated with crippled respiration or severe diaphragmatic pain, leukemia, pernicious anemia, violent chorea, loss of sleep, and continued emaciation. Melancholia may demand operation if the condition is manifestly growing worse, and Jewett believes that, in hysterical epilepsy, pregnancy should be interrupted. Wilmer Krusen (Therap. Gaz., Mar. 15, 1910).

The following course is recommended: Place the patient across the bed, in the lithotomy position, and with the external hand endeavor to depress the uterus through the abdominal wall until the index finger of the other hand (carefully asepticized) can be passed through the os and up to the fundus. An anesthetic is only occasionally required. Pass the finger up on the lateral wall of the uterus until it is above the ovum, at or near the opening of one of the Fallopian tubes; then pass it across the fundus to the neighborhood of the other Fallopian tube, and sweep down this wall, driving the contents of the uterus before it. In these manipulations try to avoid rupturing the ovum. If unable to remove the uterine contents in the way described, one should try the following Rotunda procedure: Take the finger out of the uterus and place it under the fundus, that is to say, in the anterior fornix if

the uterus is normal in position, and in the posterior fornix if the uterus is retroverted. Sink the other hand into the abdomen and compress the body between the two hands. The ovum is then driven out of the uterus into the vagina and removed (Jellett).

It is well to remember that there is a period between early and late abortion—say, in the latter part of the third month—when it is difficult, with the finger-tip, to make out the placenta, because it feels exactly like the endometrium. It is possible under such circumstances to make the mistake of imagining that the uterus is empty while the thin, broad placenta is completely adherent. In such a case it is better to try to remove this placenta by scraping with the finger-tip, as the use of the metallic curette under such circumstances is dangerous.

Analysis of 750 cases of abortion of the out-patient department of the Chicago Lying-in Hospital, and treated at their homes. The routine treatment adopted in the 276 cases of threatened hemorrhage was absolute **rest** in bed, with **morphine** and **codeine** every four hours, with **saline purgatives** where needed. When malposition of the uterus was present, this defect was corrected. The pregnancy was saved in 72.8 per cent. of the cases. The inevitable abortions were treated by **packing** and **curetting** with the finger when possible, using the curette only when absolutely necessary, excepting in chronic cases. All the mothers recovered.

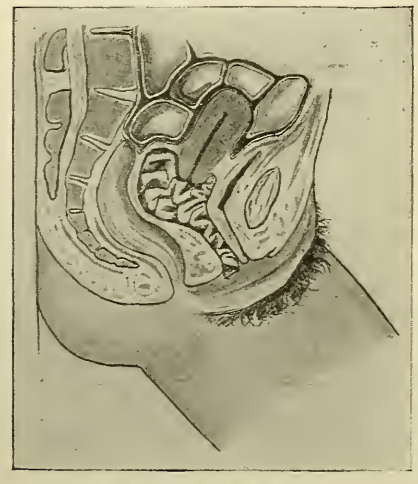
Summary of conclusions: Absolute rest was imperative; blood loss should always be prevented: cotton pledgets are preferable for tampons to gauze, being firmer; whenever possible emptying of the uterus should be done with the finger; laminary tents are difficult to sterilize; in acute abortion steel curettes are especially liable to produce abortion; curetting should always be carried out with surgical precautions; curetting is not indicated when the uterus is empty; **ergot** is indicated after the uterus has been emptied; when the uterus cavity is septic, the uterus should be emptied and disinfected; when infection has spread to the peritoneum and uterine adnexa it is best to leave the uterus alone. Stowe (Surg., Gynec. and Obstet., Jan., 1910).

The Tampon.—The vaginal tampon (or plug, as it is still termed by many in Great Britain) has been used for various obstetrical purposes for centuries.

[It is interesting to go back to the time of Smellie and to learn his clear views as to its use. We extract the following from one of his reports, slightly changed in phraseology for the sake of brevity: "In the year 1750 I was called to see a woman three months gone with child. She had been seized with flooding and had been treated for some hours. When I arrived she was exhausted, faint, and had slight pains. As the danger seemed pressing, I took the hint from Hoffmann, and stuffed the vagina tight with fine tow dipped in oxycrate (vinegar and water), which immediately stopped the discharge. I then prescribed an anodyne draught. She dozed a little, and between her dozing every now and then had slight pains, though the flooding did not return. Toward morning the pains grew so strong that the tow was forced away, together with the abortion, about the size of a goose-egg, and some coagulated blood. In such cases the strong pressure of the plug in the vagina seems to dam up the internal flooding, which, by distending the uterus, brings on labor pains." (At this time Smellie had been about thirty years in practice.) About one hundred and twenty-eight years after this, *i.e.*, in 1878, McClintock, of Dublin, in commenting on these opinions expressed by Smellie, said that he readily attributed the hemostatic effects of the plug to its "strong pressure in the vagina, damming up the internal flooding, which, by distending the uterus, brings on labor pains." McClintock goes on to say: "The occurrence of the pains which so commonly follow the use of the

plug may, perhaps, be partly due to the cause assigned by him, but this increased expulsive action is merely attributable to the influence exerted by the plug on the vaginal surface, the nerves of which part, when irritated, powerfully exciting or bearing down the contractions of the uterus." The opinions thus expressed were in accordance with the practice carried out in the Rotunda for many years before that time, and which have not been materially changed up to the present time.

These old-fashioned procedures came into disrepute in certain quarters about thirty



Vagina balléma (gauze packing).

years ago. The strenuous gynecologist with his metallic dilators and scrapers came to the fore, and introduced his modern methods, which will be referred to again. We believe that treatment by tamponade is the safest and best kind in all varieties of inevitable abortion, whether complete or incomplete. A. H. Wright.]

There are two kinds of tamponade: the vaginal and uterovaginal.

Vaginal Tamponade.—In order to be efficient the vaginal tamponade should be properly done. Although it is one of the simplest of obstetrical operations it appears that in the majority of cases it is imperfectly carried out. In the first place the vagina cannot be properly plugged while the patient is lying on her back, or on her side. The patient must be put in the Sims (semiprone) position. The perineum and pelvic floor must be thoroughly retracted by a Sims speculum, and the vagina properly ballooned, so that its vault, thus distended, may be completely filled by the material used for the packing. It is only necessary to pack tightly the upper two-thirds or three-fourths of the vagina. The mistake commonly made of packing tightly the entrance of the vagina generally causes great pain, and frequently retention of urine, by pressure on the urethra.

The tampon checks the hemorrhage, dilates the cervix, assists further separation of the ovum by damming back the blood, and induces uterine contractions. The writer, like Smellie, prefers an antiseptic plug, and uses material impregnated with 5 per cent. iodoform. A simple sterile plug is introduced by some, but an antiseptic plug is better. The former becomes foul in about twelve hours, while the latter (when iodoform is used) remains sweet for two or three days. The ordinary iodoform gauze is not suitable however, because it is too coarse in texture, that is, too much like a sieve. The blood easily runs through it. Therefore, the writer prefers to use a rather fine cheesecloth impregnated with the iodoform.

[It is prepared for me by Miss Margaret Lash, as follows: Take 4 yards of cheesecloth (good quality) 27 inches wide; tear (not cut) into strips 4½ inches wide and full length; sterilize these strips, and then boil in sterile water; ring them as dry as possible (having hands covered by sterile gloves) and thoroughly saturate them in the following preparation: 8 ounces of a 1 per cent. solution of carbolic acid in sterilized water, and enough Castile soap to make suds; 3 drams and 1 scruple of iodoform

powder; mix thoroughly in sterile basin with sterilized pestle or glass rod. After thoroughly saturating the strips, wring as dry as possible, and pack the gauze strips one after another into sterilized glass jars, and seal down while moist. One strip 4½ inches wide by 4 yards long is ample for most vaginal tampons. This happens to be one-half of a square yard, that is, 3 feet by one foot and a half. A. H. Wright.]

The method of procedure for early abortion is as follows: Place the patient in the Sims position, introduce a Sims speculum, and let the assistant retract the perineum and pelvic floor (or use two fingers of one hand for such retraction, as recommended by Schauta); introduce the continuous strip of iodoformed cheesecloth, and firmly pack the vault of the vagina. In doing this one should use not the point of a sound or forceps with fine points, but something with a fairly large surface. My custom is to use the handle of a uterine sound when *packing tightly*. Continue the packing until the upper three-quarters of the vagina is filled, and then allow the end of the strip to hang out at the vulva. If in a few hours strong pains occur, indicating that regular uterine contractions are taking place, take hold of the end of the strip and pull out the material forming the plug. It may be that by this time the ovum has been separated and expelled from the uterus. If such pains do not occur remove the tampon in twenty-four hours. There will then probably be some slight dilatation of the os, but not enough perhaps to allow the introduction of the finger. Introduce a second tampon as before. The tamponade may be kept up with safety for many days (a week or more) if the plug is renewed every twenty-four hours. It is unnecessary for the first two or three days to introduce any of the iodoformed strip inside the uterus, because the aim is to cause uterine contractions that will expel the entire ovum.

If it is found, after the removal of the second or third tampon, that the os and cervical canal are sufficiently dilated to allow the introduction of the finger, we may explore the interior of the uterus, as recommended in connection with the expectant plan, and endeavor to remove the complete ovum. If, however, a portion of the ovum has come away, the uterovaginal tamponade becomes the proper procedure.

It may be well now to repeat that the object of the vaginal tamponade is to cause the expulsion of the entire ovum during early abortion, that is, before the complete placenta is formed. The object of the uterovaginal tamponade is to empty the uterus in case of incomplete abortion (whether early or late), and also in case of late abortion, that is, after the complete placenta has been formed.

Uterovaginal Tamponade.—This procedure is divided into two stages: 1, the packing of the uterus; 2, the packing of the vagina. In packing the uterus it is generally more convenient to place the patient on her back in the lithotomy position, on a couch, on a table, or across the bed. Introduce a weight speculum, seize the anterior lip of the uterus with a volsellum forceps, and use slight traction. Ordinary iodoform gauze one-half to one inch wide is now pushed as far up as possible into the uterine cavity, employing a fine curved pair of uterine forceps, a uterine gauze packer, or a uterine sound to do so.

In order to carry out the second

stage of the operation the patient is placed in the Sims position, and the end of the narrow strip, the greater portion of which has been passed into the uterus, is tied to the wider strip used for the vaginal tamponade. After retracting the perineum and pelvic floor, the upper three-fourths of the vagina is packed tightly in the manner previously described.

If strong uterine contractions occur the double plug and ovum may be expelled together. If no strong uterine contractions commence withdraw tampon in twenty-four hours, and introduce a new one. This procedure means, of course, that the membranes will be punctured, if they were not previously ruptured. This is suitable for all cases of abortion between the end of the third and the end of the seventh month. In the seventh month we must consider the possibility of the expulsion of a living child. In helping delivery during this month, and sometimes in the fifth or sixth month, one may introduce a gum elastic bougie (English No. 12) within the uterus or a medium-sized rectal tube (H. U. Little), as recommended by Krause, and follow with the vaginal tamponade. However, the introduction of the gauze through the cervical canal and into the lower uterine segment, with the vaginal tamponade, is generally quite sufficient to produce efficient uterine contractions.

The best method to adopt to incur little risk for the patient: No interference is necessary in ordinary cases except in cases of severe anemia produced by a profuse hemorrhage or by long-continued slighter bleeding, when portions of the ovum are retained, and in cases which have become septic. The most rational method of arresting hemorrhage is to remove the ovum completely. If this has left the body of the uterus, and is retained partially or totally in the cervix or vagina, a speculum should be introduced, and, if the finger cannot easily complete the removal, ovum forceps may be used. When the ovum is still in the body of the uterus, one or two fingers should be introduced, and—while counterpressure is exercised by the other hand from the abdominal wall—the sac separated completely from the uterine wall. Once it has been separated, it can usually be removed by combined action of the internal finger and expression from without. The whole process can be made more easy if one seizes the anterior lip of the cervix with volsellum forceps (double-toothed), and administers an anesthetic. The operator must not be disturbed by the hemorrhage, but must rely on the fact that this will cease on completion of the abortion. If the cervix is not permeable for the finger, thorough plugging of the uterus, cervix, and vagina with sterile iodoform gauze is then indicated. The cervix is brought into view with a Sims speculum, the direction of its canal is ascertained by means of a uterine catheter or sound, and the size of the uterus by bimanual examination, and not by the sound. The vagina is to be thoroughly irrigated, cleansed, and dried, and then the strips of gauze introduced with smooth ovum forceps. All one's efforts should be directed toward keeping the ovum intact. At times it may be necessary to substitute a sound for the forceps in packing the uterus. If the ovum is not cast out after twenty-four hours, the plugging is to be removed, the passage again thoroughly disinfected, and a second packing undertaken. Sellheim (Münch. med. Woch., March 11, 1902).

The treatment of abortion is considered by the writer under three heads: (1) imminent abortion may be prevented by absolute rest in bed and the use of drugs like **codeine** and **viburnum prunifolium**; (2) progressing abortion, and (3) incomplete abortion may be assisted to a spontaneous termination by a hot vaginal **antiseptic**

douche and vaginal **gauze packing**. An oxytocic should be administered internally. If the result is not satisfactory after twenty-four hours, the partially dilated cervical canal should be packed with gauze and the vagina below tightly filled with the same material. Uterine contraction will thus be usually incited and everything expelled. If too much bleeding is going on, the uterus may be emptied with the finger or placenta forceps, and **ergot** administered, two or three doses usually sufficing. H. J. Boldt (Jour. Amer. Med. Assoc., Mar. 17, 1906).

Table containing the kernel of the operative indications. If conscientiously followed, it will, the writer believes, lead to considerable improvement in the practitioner's treatment of abortion and miscarriage.

OUTLINE OF TREATMENT IN ABORTION AND MISCARRIAGE.

	First Six Weeks of Pregnancy.		Seventh to the Thirteenth Week.		Fourth to the Sixth Month.	
	Cervix closed.	Cervix open.	Cervix closed.	Cervix open.	Cervix closed.	Cervix open.
Ovum retained.	Cervical and vaginal tamponade.	Removal with one finger.	Cervical and vaginal tamponade.	Removal with one finger.	Tamponade or dilate with small Voorhees bag.	Removal with two fingers.
Ovisac or placenta retained.	Uterine tamponade.	Removal with ovum forceps under guidance of finger.	Uterine tamponade.	Removal with one finger.	Tamponade or dilate with finger.	Removal with one or two fingers.
Placental pieces or decidua retained.	Dull curette.	Dull curette.	Dull curette.	Dull curette under guidance of finger.	Curette carefully or dilate to admit finger.	Removal with one finger.

F. J. Taussig (Surg., Gynec., and Obstet., May, 1909).

For several years the writer has been in the habit of injecting **adrenalin** into the uterine cervix in cases in which there was bleeding after abortion with retention of the placenta. It not only controls the bleeding, but aids in the expulsion of the placenta. He believes that the method is safe and efficacious, and prompt in its influence. Two to three drops of adrenalin solution mixed with 1 c.c. of physiological salt solution is injected. Of course, careful asepsis must be maintained. In giving the injection it is best to use a Sims speculum. If results are not prompt, the injection may be repeated in a few minutes. Grasser (Centralbl. f. Gynäk., Nu. 25, 1909).

Conclusions based on the results in 2000 cases of miscarriage: 1. Spontaneous emptying of the uterus takes place in but about 13.2 per cent. of all miscarriages. 2. The likelihood of a miscarriage to complete itself increases with the duration of pregnancy. 3. When it becomes necessary to use artificial means to complete the miscarriage, the finger followed by the curette in later miscarriages, and the curette alone in the earlier months of pregnancy, has given uniformly satisfactory results. 4. Experience has shown that where the cervix is extremely rigid it is better to introduce the curette and break up the fetus and placenta and remove them piecemeal than to attempt to dilate the cervix sufficiently to introduce the finger. 5. Packing the vagina and lower segment of the uterus is an unsatisfactory and often unsuccessful method of emptying the uterus. No success whatever was obtained in treating incomplete miscarriages in this way. 6. Pack-

ing is, however, of great value in two classes of cases: First, in exsanguinated patients to stop the hemorrhage and give the woman a chance to recover somewhat from the loss of blood before emptying the uterus. Second, when the cervix is very rigid, a tight cervical pack for twenty-four hours will soften it so that dilatation may be attempted with safety. 7. The results of artificial methods are as good as, but not better than, where nature has succeeded in emptying the uterus. 8. Artificial methods are necessary in a majority of cases, however, simply because nature has failed. 9. In infected cases the essential thing is to get rid of the infectious material by emptying the uterus, the particular method employed making little difference. 10. The later in pregnancy miscarriage occurs, the smaller the liability to become infected, but the greater the likelihood of developing grave septic complications if infection does take place. 11. The mortality is practically the same at all periods of pregnancy. 12. Induced abortions have a greater mortality than accidental. The mortality of patients admitted to the hospital after criminal abortions was 10 per cent. E. B. Young and J. T. Williams (Boston Med. and Surg. Jour., June 22, 1911).

Treatment of Incomplete Abortion.—Some authors state that the uterus may be emptied at once, the cervical canal being dilated and the finger or curette or both being used. Occasionally the finger may be used with advantage when the cervical canal is well dilated, but we do not advise the use of the curette. Others hold that we should not interfere until there is decomposition of the ovum or dangerous hemorrhage. We do not approve of this kind of expectant treatment.

Without discussing these or other methods of treatment we recommend the **uterovaginal iodoform tamponade** for all kinds of incomplete abortion, whether occurring before or after the formation of the placenta. In these cases there is nearly always some dilatation of the cervical canal, generally enough to allow the introduction within the uterus of a narrow strip of iodoform gauze. If the canal which was once slightly dilated has again become so contracted that no gauze can be passed through it we may do the vaginal tamponade as before directed, and thereby cause sufficient dilatation for our purposes. If we use the iodoform gauze or cheesecloth instead of ordinary sterile gauze, we do not fear the danger of decomposition which is said by some to occur in the uterine cavity about the vaginal plug. If, however, one fears such an occurrence he should remove the vaginal plug in ten or twelve hours, instead of waiting twenty-four hours, as we have generally recommended. The uterovaginal tamponade may be repeated several days if considered necessary.

If after waiting one or two weeks the accoucheur has reason to fear that some portions of the egg have been retained, and there are no signs of sepsis, he may use a dull curette with great care.

Sepsis with incomplete abortion is a very serious complication. The curette, whether dull or sharp, should never be used when there is septic endometritis or even saprophytic infection. The finger may be used very gently to remove *débris* when the cervical canal is sufficiently dilated. Then use an intrauterine douche of warm **salt solution.** After the douche is used introduce iodoform gauze (the coarser, the better) into the uterus, and place a certain amount in the vagina without packing tightly. Leave

this in six hours, and then remove. After this removal keep the patient as much as possible in Fowler's position, that is, a half-sitting position, to facilitate drainage. Apart from such local treatment carry out the usual line of treatment recommended for puerperal infection.

Method of dealing with an infection after an abortion. The cavity of the uterus is first cleaned out to prevent the continued absorption of toxins from any infectious material which may be present, and thus, at least, limit the intensity of the process. For this the finger alone is employed, or combined with the curette. The cavity of the uterus is washed out with hot saline and 2 ounces of **peroxide of hydrogen;** it is then cleansed with **saline solution** and sponged dry. After this 2 or 3 drams of **iodoform** powder are placed in the uterine cavity, which is then packed with sterile gauze. Now the *cul-de-sac* is freely opened, and, after evacuating any fluid which may be present, it is irrigated with hot saline, followed by 2 ounces of peroxide of hydrogen. This in turn is washed out and the cavity wiped dry. Last, 2 or 3 drams of sterilized iodoform powder are dusted into the *cul-de-sac,* after which it is packed tightly with strips of sterile gauze.

By this procedure the author believes that two advantages are obtained: (1) by evacuating the fluid from the *cul-de-sac* further absorption is prevented; (2) the ovaries and Fallopian tubes are saved by preventing adhesions which would almost invariably form as a result of the organization of the exudate. Personal experience has shown that the secretions from the uterine cavity are almost always sterile, while organisms are invariably found in the exudate in the *cul-de-sac.* Hunter Robb (Amer. Gyn., June, 1903).

Continuous or frequent **irrigations** urged to prevent absorption from the lochia and thereby the production of the toxemic element of puerperal sepsis. Weil (N. Y. Med. Jour., May 18, 1911).

When a septic abortion is recognized it must first be determined that the infection has not extended beyond the uterus before active treatment is instituted. When the diagnosis of septic abortion has been confirmed and the disease is confined to the uterus the next procedure of the physician should be determined by the bacteriological examination, except when there is considerable hemorrhage; in these cases immediate curettage is indicated. If the bacteriological examination reveals the presence of streptococci, staphylococci, bacteria coli, or the ordinary saprophytes **curettage** should be practised and no serious results are to be expected. But if the examination reveals the presence of hemolytic streptococci, especially if in pure cultures and with distinct hemolysis, the writer advises against any local intervention, as the danger involved is very great. The treatment should be general, to increase the power of resistance of the organism in the expectation that the infection will be overcome by local reaction. **Ergotin** treatment is indicated to limit absorption through a firm contraction of the uterine wall and at the same time favor expulsion of the remains of the fetus. Winter (Med. Klinik, April 16, 1911).

Winter's advice not to interfere in septic abortion, except in the case of hemorrhage, until several weeks have passed, all symptoms of infection having disappeared, and the uterus is not completely empty, is only valid in one respect, viz., the liability of multiple infections from curetting, a sharp rise in temperature nearly always following the operation. Many cases would terminate fatally, however, were it not for timely curetting. Many conservative gynecologists confine themselves to forceps, sponges, or the finger and never use the curette. Le Bovis (Semaine méd., July 26, 1911).

Curettage and Emptying the Uterus at a Single Sitting.—This operation may be occasionally justifiable when there appears to be urgent need of rapid emptying of the uterus. Whether this be true or not it is

recognized as a legitimate operation by some of the best obstetricians and gynecologists in the world. A brief description of the procedure is therefore given. Anesthetize the patient, place her in the lithotomy position "across bed," preferably on a Kelly pad. Prepare external parts and vagina as for vaginal hysterectomy, using especially green soap and hot water, and a hot solution of lysol or other germicide. Introduce a weight speculum, secure the anterior lip of the cervix with volsellum forceps, introduce a branched steel instrument into the cervical canal, and dilate; then introduce a curette into the interior of the uterus and scrape out its contents. Some operators then wash out the interior of the uterus with an antiseptic solution, while others use the uterine iodoform tamponade.

Two hundred and seven cases personally treated with **curette.** Sequelæ were met with in 34.4 per cent., compared with 92.4 in those in which it was not employed. In the former, the menses were regularly re-established in 60 per cent., pregnancy to term supervened in 53 per cent., abortion recurred in only 13 per cent., and sterility prevailed in 32.3 per cent. When the curette was not used and fingers were, regular menstruation in 39.4 per cent., pregnancy to term also in 39.4, repeated abortion in 47.3, and sterility in 25.1. The cases were all treated upon the same general principles, and the curette was only employed in the presence of the strongest indications. Schaeffer (Deut. Prax., Nos. 1-3 and 5-8, 1901).

An incomplete abortion may be recognized by the bloody charge, sepsis or failure of involution as instanced by the soft, boggy uterus, the patulous cervix, and the detection during the examination of fragments of the ovum. On the other hand, if the abortion has been wholly completed, that is, if the entire uterine contents, including the hypertrophied decidua, have been completely expelled, the uterus is firmly contracted and the os is closed. The management of incomplete abortions is purely surgical, for drugs have little or no effect on the expulsion of retained portions of the ovum. Hemorrhage, sepsis and adrenal inflammations, with their complicating sequelæ, can alone be controlled and avoided by prompt aseptic **emptying of the uterus.** Here again, as in the treatment of inevitable abortions, the strictest asepsis and the most delicate skill are necessary to evacuate the uterus without traumatizing the passages. No expectant plan of treatment has given any satisfaction; the situation should be explained to the family, as well as the dangers from the possible sequelæ and the necessary operation made. J. O. Polak (Long Island Med. Jour., June, 1907).

Treatment of Criminal Abortion.— In the majority of cases of criminal abortion we have incomplete abortion with sepsis. We have to consider at the same time that some injury may have been done by the operator in his manipulations. One of the most common of such injuries is puncture of the uterine wall. The possibility of such injury should make us doubly careful in our methods of treatment.

In performing an autopsy upon a woman who is supposed to have attempted abortion search should be made for the embryo or pieces of it, or for the placenta. If the uterus is empty, the thickness of its walls must be measured, and the insertion of the placenta sought, as this can be recognized up to the tenth day after the expulsion of the embryo. This is possible even later, if the uterus is kept in 90 per cent. alcohol. The examination of the ovaries is of only relative importance, as no positive signs exist there. Stains of meconium, if found, will prove the abortion. If an instrument has been used to cause abortion, traces of the damage done by it will

be seen. This is especially true when the uterus has been perforated. Brouardel (Jour. des Praticiens, Jan. 12, 1901).

Six hundred and ninety-eight cases of abortion witnessed, supposed to be spontaneous. Four of the women died, that is, 0.57 per cent. During the same period 44 cases of criminal abortion were treated; the mortality was 56.8 per cent., that is, only 19 women recovered. In the presence of a complete or incomplete abortion, due unmistakably to mechanical measures, or even when such abortive measures are suspected, and in absence of any complication, early evacuation of the uterus is required. If septic accidents have already developed, evacuation is still more urgent, and general measures are also indicated. Maygrier (L'Obstétrique, July 4, 1902).

When the patient is kept in an aseptic condition, that is, without local examination or other maneuvers, and hot douches are given only in numbers sufficient to combat alarming hemorrhage, the temperature keeps within normal range. Careful watching may show a slight rise; at the same time slight hemorrhage may recur or a very slight fetid odor may be noticed in the secretions. These signs show that the fetus is dead, that the placenta has become a foreign body, and that the uterus is trying to expel it. This is the time for **curetting** if spontaneous expulsion does not rapidly follow. At this time the operation is easy and without danger. In case of primary uterine infection with temperature above 38°C., the curette should be used at once. It is easy to order injections at 45° or 48° C. (113° or 118° F.), but they are generally given tepid and thus only aggravate the tendency to hemorrhage. Each **douche** should be preceded by a careful toilet of the external genitals. In curetting wait until the uterus contracts, curetting gently during the period of relaxation after a contraction, and using the largest curette possible. Curette at the moment when the placenta is almost entirely separated and the uterus offers a thick and resisting wall. Perforation may well be feared when there is infection in the uterus, for then one's hand is forced and the curetting may be done while the placenta is still too firmly adherent. De Bovis (Semaine méd., No. 43, 1910).

Treatment of Patient with "Aborting Habit."—When we have treated a certain patient for two or three threatened abortions which have become inevitable, the presence of syphilis should be carefully inquired into. If there is a syphilitic taint, or even a suspicion of it, both patient and husband should be placed under constitutional treatment. Malformations, displacements and other abnormalities of the uterus, and other conditions which act as direct causes of abortion may, of course, prevail in these cases, and should be carefully sought after.

Two cases in which the writer was able to correct a tendency to habitual abortion by the systematic introduction into the uterus of a **suction cannula.** It not only induces hyperemia in the organ, but stimulates it to muscular contractions, this exercise aiding in restoring normal conditions. In the first case he applied the cannula for half an hour at a time, at twenty sittings in the course of seven weeks; in the second case the cannula was left for ten hours at a time, the procedure being repeated eight times in the course of one month. Both women have since borne healthy children, although there was a history of five and three abortions, respectively; the patients were 27 and 23 years old. Turan (Deut. med. Woch., May 5, 1910).

Apart from such considerations, **rest** and **quiet** are the important elements in the treatment of such cases. The patient should be kept in bed or on a lounge from two days before the time of menstruation until three days after it ceases. In addition, if the patient is restless or sleepless, she

should receive enough **opium** or other hypnotic, such as **veronal**, to make her sleep at least fairly well every night. During intervals she should have a moderate amount of **exercise in the open air**, and suitable **tonics**. Strong purgatives, vaginal douching, sports, and all kinds of fatiguing work should be carefully avoided. In case of retroversion or retroflexion, the displacement should be corrected, introducing, if necessary, a suitable **pessary**, and leaving it until about the end of the fourth month.

ABERRANT FORMS.—The recognition of such conditions obviously is of great diagnostic importance.

Missed Abortion.—The retention of the ovum within the uterus after its death is thus termed. The death of the ovum may occur before or after the formation of the placenta, but it is most apt to happen in the third month. This is probably due to the fact that at that time the egg is to some extent loosened on account of the atrophy of a large portion of the chorionic villi. The death of the fetus frequently occurs, however, in the fourth, fifth, sixth or seventh month, and in a certain proportion of these cases the abortions are "missed."

> The term missed abortion is inappropriate, as it is used as a synonym for delayed abortion. The period from the death of the fetus until it is extruded is unusually prolonged, and it undergoes important changes — those due to a cessation of vitality. This period may be devoid of symptoms, and as a rule the embryo has been dead some weeks or months before the patient comes under observation. J. Oliver (N. Y. Med. Jour., Dec. 3, 1904).

It is a singular fact, in connection with a case of missed abortion, that the dead ovum frequently or generally remains in the uterus quiescent until term. In some cases the dead ovum still remains quiescent for an indefinite time, even after term. Although we cannot speak very definitely, we know that the dead ovum may remain in the uterus without any change in structure for one, two or more years. At least such appears to be the opinion of the majority of obstetricians at the present time.

> Case in which a dead fetus had been carried *in utero* for probably six and a half months without causing physical disturbance. One month after the last menstrual period, she began to show symptoms of pregnancy, morning sickness, enlargement of the breasts, etc. At about the fifth month from the time her menses ceased she commenced to look for signs of "life," which did not appear. Ascribing her symptoms to early menopause, she ceased to give herself a thought about her condition, gained in weight, and felt quite comfortable. On March 12, 1911, at about 3 A.M., she commenced to have cramp-like pains and expelled a sac which on examination proved to be a fetus of about three and a half months, with cord and placenta connected. Microscopically the placenta showed a fatty degeneration of the entire mass. The fetus was of a dark and brownish black. Ohlbaum (Med. Record, Aug. 26, 1911).

[This fact is sometimes of great importance from a medicolegal standpoint. The case of Kitson *vs.* Playfair, which was tried in England about fourteen years ago, created intense interest. Dr. Playfair, the distinguished teacher and writer on obstetrics and gynecology, while treating in an ordinary professional way Mrs. Kitson, the wife of Mrs. Playfair's brother, emptied the uterus, and found something like fresh placenta. Examination under the microscope confirmed his suspicion, and he expressed the opinion that there had been a recent incomplete abortion. As Mrs. Kitson had not seen her husband for over a year (he being in India and

she in England) this meant a charge of immorality. Dr. Playfair informed his wife, and Mrs. Kitson was dismissed in disgrace from her ordinary circle of relatives and acquaintances. The husband in consequence entered action against Dr. Playfair. At the trial several leading obstetricians agreed with Playfair, while others took the opposite view, and said the substance removed might have been the result of a conception at least eighteen months before. The case was decided in favor of Mrs. Kitson, and Playfair was compelled to pay a large amount for "damages." The suit cost him altogether over $50,000. We may add that many at the time of the trial thought that, even if Dr. Playfair had been correct in his contention, he was not justified in revealing a professional secret. A. H. WRIGHT.]

Mole.—When the dead ovum or a portion of it is retained in the uterus it is called by many a mole. When there has been extravasation of blood between the layers of the membranes or into the substance of the decidua, coagulation takes place and the mass with its clot or clots is called a "blood mole." When there has been repeated extravasation of blood within the ovum the blood-strata undergo partial organization and the mass is called a "flesh mole." This flesh mole retains to some extent its attachment to the uterine wall, and in some cases after partial detachment may form new attachments. Under such circumstances the detention of the mass within the uterus may be much prolonged, as before mentioned.

> The fleshy mole is undoubtedly a form of the process known as "abortion," but the obstetrician should remember that the pathological changes which produce it may occur at very different stages of pregnancy. The precise time at which the arrest of normal pregnancy occurs cannot always be determined by examination of a fleshy mole. Neumann (Monats. f. Geburt. u. Gyn., Feb., 1897).
>
> In tuberose fleshy mole, abortion is produced in the following manner: There is an undue blocking of the serotinal sinuses in the large-celled layer, leading to a slow engorgement of the intervillous circulation. This will bulge out the choriobasal septa, and, as these tack down the chorion at definite points, the amnion and chorion will bulge up between. This produces the tuberose swellings. The embryo dies as the result of this interference with the circulation, and its death is "secondary." The placenta becomes a thrombosed mass and is retained a certain time before expulsion. The primary link in the chain of events is the excessive clotting in the serotinal sinuses from a cause as yet unknown. D. Berry Hart (Jour. of Obstet. and Gynec. Brit. Empire, May, 1902).

Treatment of Uterine Flesh Mole.—There is far from a consensus of opinion as to the treatment of such a mole. Some say leave it alone if there are not disturbing symptoms; others say empty the uterus at once when a diagnosis is made. It happens that a diagnosis is frequently difficult or impossible, and it also happens that in the majority of cases the mole is expelled from the uterus within a reasonable time. The general practitioner will be on the safe side not to interfere unless serious symptoms arise. If very serious symptoms do appear he should at once do the uterovaginal tamponade as before recommended.

Hydatiform Mole (syncytioma benignum, vesicular mole, myxoma chorii).—This is a vesicular tumor within the uterus formed by simple hyperplasia or cystic degeneration of the villi of the chorion at any time during pregnancy, but most frequently in the early months, and often after abortion.

The accoucheur, in considering the symptoms of a supposed abortion,

should ever keep in view hydatiform mole and chorion epithelioma, because early diagnosis and prompt treatment of both neoplasms are so extremely important. The first symptom of the former is a discharge of a bloody fluid which is sometimes said to resemble currant juice. Our first suspicion is generally threatened abortion. If the discharge becomes more watery in appearance, if vesicles are expelled, or if the uterus increases abnormally in size, we should suspect a vesicular mole. Generally we have to be guided by two symptoms, hemorrhage, and abnormal increase in the size of the uterus.

Treatment of Hydatiform Mole.—The condition is serious and prompt treatment is required. The uterus should be emptied as soon as possible. The following is recommended: **Dilate** the cervical canal with Hegar's dilators, then introduce a **sea-tangled tent,** then **plug** the vagina as before described. If strong uterine contractions come on within a short time remove the tampon and tent. If such contractions do not come on remove the tampon and tent in twenty-four hours, then do the **uterovaginal tamponade** as thoroughly as possible. This will, as a rule, be sufficient to cause efficient uterine contractions which will expel the mole. If there is any doubt as to such expulsion explore with the finger gently, and **scrape** the uterine wall with its tip. The metallic curette is especially dangerous in this case because the uterine walls are more or less weakened by the invasion of the cystic villi. Occasionally it may be advisable to use a dull curette, but this should be considered a misfortune, and great care should be exercised.

Chorioepithelioma (chorion epithelioma, syncytioma malignum, deciduoma malignum, choriocarcinoma).—This is a very malignant form of epithelioma developed from the epithelial layers covering the villi of the chorion. It is usually associated with abortion, and in 50 per cent. of the cases is preceded by hydatiform mole. We are told that it may occur after labor following full term, but the writer has not met such a case. Obstetricians have for some time considered that this form of epithelioma is always associated with pregnancy. Some surgeons have said recently that tumors simulating chorion epithelioma have been found not only in women in the absence of pregnancy, but also in men, and that all such have arisen in pre-existing teratomata. Obstetricians, however, do not believe that such tumors are really chorioepitheliomata. Metastatic deposits, even more malignant than the original tumor, soon appear in various parts of the body, especially in the vagina and lungs.

Hemorrhage is the earliest and most persistent symptom. The flow is at first red, but soon becomes dark and offensive. The uterus grows rapidly and is often perceptibly soft in one or more places. A hemorrhage is serious when it becomes in the slightest degree offensive. Scrapings from the uterine wall may be examined microscopically.

Treatment of Chorion Epithelioma.—A radical operation is immediately indicated. The uterus, appendages, and metastatic deposits, especially if any be found in the vagina and vulva, should be removed.

INDUCED ABORTION.—Induction of abortion is very grave in any

case, and *should never be decided on without a consultation.*

Indications.—It may be said in a general way that, in any case where the life of the patient is imperiled by the continuation of pregnancy, abortion should be induced. In nearly all cases, however, when serious disease is present it should receive prompt and careful treatment. That death of the embryo or fetus is a positive indication for the induction of abortion need scarcely be emphasized.

Tuberculosis.—It was a few years ago (and is now we fear) the custom of some physicians to induce abortion in all pregnant women suffering from tuberculosis. We have to consider, however, that in the light of our present-day knowledge tuberculosis is a curable disease in the pregnant woman as well as in the non-pregnant one. If, then, our patient has tuberculosis during pregnancy it is our duty to treat the tuberculosis and not to murder the unborn child. This should be our general rule. In a few exceptional cases (and they are very few), especially when the morbid process is far advanced, the uterus should be emptied.

Cardiac Disease.—In a large majority of women who have heart disease, pregnancy does not produce effects sufficiently serious to justify the induction of abortion. If, however, as happens in a small proportion of cases, especially when there is mitral stenosis, such symptoms as hemoptysis, precordial distress, palpitation, and great debility appear, and grow steadily worse, under appropriate treatment, the induction of abortion should be considered.

Excessive Vomiting of Pregnancy.—We have recently learned that the pernicious vomiting of pregnancy is due, in some cases at least, to peculiar disturbances of metabolism which produce a toxemia. Chemical examination of the urine shows a decrease of the amount of nitrogen excreted as urea, and an increase of the amount excreted as ammonia. In normal pregnancy, the quantity of ammonia excreted (the ammonia coefficient) is 4 to 5 per cent. In pregnancy with this form of toxemia, it may rise to 10, 20, or 40 per cent., or even higher. Williams thinks that when the ammonia coefficient exceeds 10 per cent. the pregnancy should be immediately terminated. We have found, however, that in some cases the ammonia coefficient may considerably exceed 10 per cent., and the patient may recover without the termination of pregnancy. It is hoped that further investigation will lead to conclusions which we shall all accept. We agree with Williams to some extent, however, and believe that when the ammonia coefficient reaches 10 per cent. the patient is in a dangerous condition, and needs prompt and suitable treatment. If in spite of such treatment carried out for one to two weeks she grows steadily worse, pregnancy should be terminated.

The practitioner who does not depend on this chemical test should be guided by the symptoms and condition of the patient. Indeed no one should neglect a careful study of all symptoms. It is very important that we should not wait too long. We have certainly much to learn yet respecting this very perplexing subject. We have occasionally found that the results of interference even in apparently favorable cases are sadly disappointing.

In *hyperemesis* with marked and progressive exhaustion, especially as indicated by weekly loss of weight, when the usual dietetic and medicinal measures have failed, no time should be lost in emptying the uterus. Under the combined effects of toxins and starvation the woman's strength fails insidiously and often the end comes abruptly. Lives are lost by too long delay. Serious complications, advanced cardiac disease and certain others, emphasize the necessity for intervention. Jewett (N. Y. State Jour. of Med., Mar., 1908).

General Toxemia of Pregnancy.—No definite statement can be made as to the exact time when interference is desirable in case of general toxemia of pregnancy. Apart from excessive vomiting in connection with toxemia we fear especially eclampsia. Before the onset of convulsions the induction of abortion is very rarely considered necessary. Convulsions, as a rule, do not occur in the early months of pregnancy; when they occur in the later months an immediate delivery is considered necessary. A vaginal Cæsarean section is probably safer than rapid dilatation of the cervix with quick extraction. Both operations, however, are serious, and the careful, conservative physician will prefer to resort to safer procedures. The importance of great haste in emptying the uterus has been grossly exaggerated in recent years. We think this is especially true as to eclampsia.

Chronic Nephritis. — Induction of abortion is not, as a rule, indicated in cases of chronic nephritis. Occasionally the symptoms grow so serious, in spite of suitable treatment, that the patient's life is endangered. Under such circumstances the uterus should be emptied. Disorders of vision during pregnancy are very serious in patients who have chronic interstitial nephritis. Partial or complete blindness in such cases generally indicates a fatal termination. On the other hand, one may have absolute blindness due entirely to a state of autointoxication. In such a case the ophthalmic changes are not marked as a rule, and the sight generally returns soon after the uterus is emptied. Herringham (Brit. Med. Jour., May 7, 1910) states that this transient form of blindness is never found in uremia or associated with chronic interstitial nephritis.

Retinitis.—Affections of the eyes should be carefully studied. Retinitis should receive prompt attention. If the symptoms grow worse instead of better after treatment for a few days, interference may become necessary. In cases of retinitis with white plaques, and dimness or loss of vision, associated with serious albuminuria, abortion should be induced at once. Colin Campbell (oculist) agrees with Herringham and various modern pathologists as to the great difference between a retinitis due to an old chronic nephritis and a retinitis caused by autointoxication of pregnancy. He says the retinitis of pregnancy has a bright outlook compared with that of nephritis. Examination of the urine will materially aid a coming to an understanding of the condition. "In pre-existing nephritis the quantity is usually greater, the urea and nitrogen more nearly full normal, and the albumin and casts more abundant. In pre-eclamptic cases the uric acid and the amidoacids are markedly increased" (Can. Jour. of Med. and Surg., Oct., 1910). It may be stated in a general way that such untoward symptoms occurring early are much more serious than similar

symptoms which may appear late in pregnancy.

Pyelitis.—Pyelitis due to toxemia of pregnancy is not very uncommon, although, until recently, it was not recognized as a separate entity. Interference with pregnancy is not generally required. If, however, the temperature keeps above normal for four weeks; if there is much pus in the urine; if the leucocyte count is high, abortion should be induced. It is better if possible, however, to defer interference until the child has become viable.

Ante-partum Hemorrhages.—Hemorrhage from placenta prævia is our chief concern in this connection. If interference becomes necessary we should employ the **vaginal tamponade,** and should never dilate the cervix to the slightest degree. If the hemorrhage is increased by complete or partial separation of a placenta normally situated the same rule as to treatment applies. Such hemorrhages do not occur frequently before the child is viable, and, consequently, need not be discussed in detail here.

Retroflexion of the Uterus.—When serious symptoms appear because of retroflexion or retroversion of the uterus, and the misplacement cannot be corrected, it may become necessary to interfere. In the majority of such cases abortion takes place without any interference.

Contracted Pelvis.—The induction of abortion in cases of contracted pelvis was for a long time considered indicated. We hope it is generally conceded now that such a procedure is both incorrect and sinful. We have learned in recent years that conservative **Cæsarean section,** done at the proper time with reasonable care and skill, is one of the safest and best operations now known to surgery. Such having been demonstrated, we have done well in ceasing to destroy unborn children because of contracted pelvis.

Hydramnios.—When the hydramnios causes the distention which seriously affects the mother's health we may have to consider the desirability of emptying the uterus. In such cases, however, we can generally wait until the child becomes viable.

Appendicitis, Ovarian Tumor, and Other Abdominal Growths.—Abortion should not be induced for any of these conditions. The ordinary operation for the disease or new growth should be performed.

Goiter.—As a rule there should be no interference, at least until the child is viable.

Myoma Uteri.—No interference with pregnancy is indicated as a rule. In a limited proportion of cases one or more fibroids may be so situated that delivery in the ordinary way is a physical impossibility; but, even under such circumstances, the induction of abortion is very rarely indicated. We may, however, meet a uterus in which the growth would interfere with normal delivery, but in this case the child might be delivered by Cæsarean section if pregnancy went on to term. Women with very bad fibroids seldom conceive, and when they do early abortion is apt to occur.

Chorea.—In a certain proportion of severe cases of chorea the patient goes from bad to worse, notwithstanding suitable treatment. In very serious cases the woman grows worse very rapidly and dies unless the uterus is emptied. In many cases this serious procedure, unfortunately, does not save the patient.

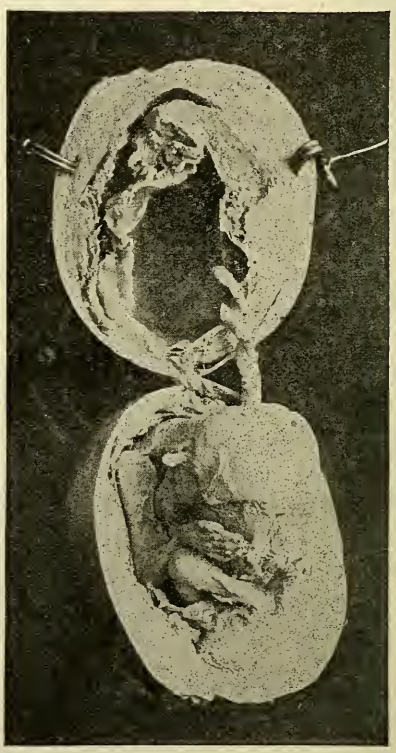
The induction of an abortion justifiable in pernicious *hyperemesis,* in some cases of chorea, in certain forms of convulsive seizures, nephritis preceding or manifesting itself early in pregnancy, and in certain cases of contracted pelvis. If the well-known bougie method does not bring about the desired result in from twenty-four to forty-eight hours, it may be supplanted with a tampon of gauze carried into the uterine interior. H. J. Boldt (Jour. Am. Med. Assoc., Mar. 17, 1906).

Method of Inducing Abortion.—For the induction of abortion we employ the methods and procedures generally used

Amnionic sac containing embryo and waters. The thick decidua retained in uterus. (Seven weeks.)

in cases of inevitable abortion (see p. 165). When speaking about the treatment of the latter we had in view the fact that nature, chiefly through uterine contractions, and hemorrhages, had done something, perhaps much, in the process of abortion. The ovum has been more or less loosened from its attachments, and the cervix has perhaps been more or less dilated. In considering the induction of abortion, we assume, on the other hand, that the ovum is pretty firmly attached to its moorings, and that the cervical canal is not dilated. Under such circumstances it is more difficult to empty the uterus. The following recommendations are made for the induction of abortion at different periods of pregnancy up to the seventh month. This course seems advisable, although it will mean a certain amount of repetition:—

In any case prepare the patient as for vaginal hysterectomy, or as before described, for curettage (see p. 173).



Pregnancy, three months, showing fetus below. Placenta formed.

First or Second Month.—Introduce a vaginal tampon of iodoform cheesecloth as before described. This may be removed, and reintroduced, every twenty-four hours for five or six days. In many cases these vaginal tampons will not produce the desired result, even in five or six days. Under such circumstances one may introduce a narrow strip of iodoform gauze within the uterus after the first or second day. If, in doing this, one punctures the mem-

brane, no serious harm will be done. After such introduction, practise vaginal tamponade. It may be necessary to do more than the introduction of the gauze; if so, adopt the old-fashioned method of introducing a uterine sound, and purposely puncture the membranes if possible. This is suitable, especially in cases of pernicious vomiting, because such puncture allows the escape of the liquor amnii, and such escape often causes the serious symptoms to subside immediately. It happens that in certain cases it is difficult to puncture the membranes because the deciduum is thick, tough and elastic.

Third Month. — Carry out the methods recommended for the first and second months. There is less chance of causing the expulsion of the entire ovum and on that account it is not well to wait long before invading the interior of the uterus.

Fourth and Fifth Months.—Practise a uterovaginal tamponade as before described as rapidly and thoroughly as possible.

Sixth and Seventh Months.—Introduce a vaginal tampon, remove in twenty-four hours, place patient in lithotomy "across bed" position: introduce a weight speculum, seize the anterior lip of the cervix, pass a gum-elastic or hard-rubber bougie, or a medium-sized rectal tube within the uterus, between the membranes and uterine wall to the fundus if possible. Then place woman in Sims's position, and plug vault of the vagina tightly. Labor will generally come on in a few hours, and the uterine contents will soon be expelled. It is sometimes advisable to introduce the bougie in the fifth month.

We find that in some cases the tamponades are not efficient, and we are compelled to adopt more forceful procedures. As before mentioned we think the use of the metallic dilator and sharp curette in the "single sitting" operation is always dangerous. If this statement is true, or even half-true, it is sad to notice that some of our ablest authors in recent textbooks say that "the induction of abortion is practically free from danger if perfect asepsis is observed." This operation is especially dangerous in the class of cases included in this chapter because the patient is generally in a bad physical condition from the complication which calls for the termination of pregnancy, as, for instance, pernicious vomiting.

It is generally an easy matter, especially after a vaginal tampon has been in place twenty-four hours, to dilate the cervix with the Hegar dilators sufficiently to allow the introduction of the gauze within the uterine cavity. We also recommended the use of the laminaria (sea-tangle) tent for dilatation. It is said, however, that there is great danger of infection from the use of any tent for such purpose. There was, of course, much reason for such fear many years ago when the sponge, tupelo and laminaria tents were not sterile, and, in addition, were not used in an aseptic way; but during recent years we have been able to get excellent sterile laminaria tents that are perfectly safe if used in a cleanly way.

Similar objections have been raised against tampons because they also were unsafe as used many years ago, but the tampon medicated with iodoform or other suitable antiseptic is as safe as anything that can be introduced within the uterine cavity. It is thought by some that there is danger from the use of the bougie according to Krause's method, but, if the bougie is made per-

fectly sterile by boiling and is carefully used, the danger therefrom is very slight. It is well to remember, however, that there is always some danger in connection with any obstetrical operation through want of care on our part. We should ever make a continuous effort to guard against such danger.

A. H. Wright,
Toronto.

ABORTION, TUBAL.—

DEFINITION.—Early interruption, *i.e.*, abortion, is the natural outcome of extra-uterine pregnancy, whether by reasons of insufficient blood-supply or unfavorable mechanical conditions for the continued development of the fetus.

[A brief review of the history of this important subject ought to possess for us more than ordinary interest because of the important rôle played in its development by one almost of our own number and generation in whom we may take a pardonable local pride. I refer to the illustrious and lamented John S. Parry. He was not the first to write upon the subject. Indeed, Albucasis, the Arabian, in the eleventh century recognized and described a case of extra-uterine pregnancy. Nor was he the first to grasp the possibilities of operative treatment in the emergency of rupture. That was proposed by Harbert, of New York, in 1849. The merit of Parry consisted not only in grasping the significance of the catastrophe and the correct mode of meeting the emergency, but in applying his philosophical mind and scholarly attainments to the production of a monograph which by its masterly marshaling of facts and lucidity of deduction should have quieted the doubts of Thomas. He was able to collect for his book, which was published in 1876, 500 cases reported in the literature. Of 499, in which the result was stated, 366 died and 163 recovered. Of the deaths, 174 had been from rupture. Of these deaths 81 had died within 24 hours. These figures were his text. He began his sermon with this sentence: "From the middle of the eleventh century, when Albucasis described the first known case of extra-uterine pregnancy, men have doubtless watched the life ebb rapidly from the pale victim of this accident, but have never raised a hand to help her." Then, though not himself a surgeon, he points out the plain surgical indications. In the same year as the publication of his monograph he died, doubtless depriving the world of one who was destined to become one of its greatest figures in the advancement of medicine. Parry was a pupil of my father, who often used to speak of his studious habits and scholarly grasp. He was by nature fitted for mental leadership.

The honor of performing the first operation for this emergency went to Lawson Tait in 1883. He had been earnestly solicited to operate for this condition in 1881 by a physician who had correctly diagnosed a case of rupture with internal hemorrhage. He refused, and the patient died shortly after. Unfortunately the first patient operated on died also, but his change of heart was complete, and, correctly attributing his failure in the first case to faulty technique, he altered his method and continued to operate all such cases. Of the next 40 cases only 1 died. Truly a brilliant record which was not long in converting the medical fraternity.

The original microscopical preparations of Tait in which he demonstrated his ideas on extra-uterine pregnancy and pelvic hematocele which, before him, were in a very confused state are still to be seen in the museum of the Royal College of Physicians in London.

There are many other names of more or less importance in connection with the development of the subject, but these two are central and all we have space to consider. John B. Deaver.]

SYMPTOMS.—The symptoms of extra-uterine pregnancy include those due solely to the condition of pregnancy and those which arise only from its abnormal situation. Inasmuch as the majority of cases terminate within three months, at which ordinary signs of pregnancy are not usually pronounced, we do not often get much help from the symptoms belonging to the first group. Yet

such symptoms and signs as enlargement of the breasts, the presence of colostrum, cessation of menstruation, increased vascularity of the genitalia, softening of the cervix and body of the uterus with slight enlargement, disturbances of the bowels or bladder, morning nausea, and the abnormal appetite, cravings or sensations which the multipara sometimes recognizes, are occasionally of confirmatory value.

It would be desirable to make the diagnosis before rupture were it possible to do so. Unfortunately a large percentage of cases give such trifling evidence of the true condition, if indeed there be any prodromal symptoms at all, that no suspicion is aroused. Still it is occasionally possible to make the diagnosis and it should be our effort to do so. One operator, Baldwin, of Columbus, Ohio, has reported 11 such cases.

> A prolonged continuous blood-stained uterine discharge is an important aid in differentiating tubal abortion; even if the proportion of blood is small its persistence for two up to five weeks is characteristic, and absence of blood in the vaginal discharge is strong evidence against a recent hematocele. The slight hemorrhage seems to persist longer after tubal abortion than after rupture. Incomplete expulsion of the ovum is also liable to keep up the hemorrhagic discharge, and the writer relates some instances of such retention of the placenta with the tube open and of total retention with the tube closed. The small encapsulated collection of blood may be taken for a fibroma, and the resulting disturbances for inflammatory processes in the adnexa or in the uterus. Certain cases of tubal abortion have been diagnosed as a hemorrhagic metritis, and the uterus was curetted when this organ was sound and the trouble was in the tube beyond the reach of the curette. F. Lejars (Semaine médicale, July 13, 1910).

> A new sign of tubal pregnancy is a more or less striking paleness of the cervix. The absence of this paleness does not, however, exclude this condition, but its presence, when not due to obvious other causes, is almost pathognomonic. It is only present, however, in those cases of tubal gestation in which there is bleeding from the uterus, and only while this bleeding is actively going on. Golden (W. Va. Med. Jour., May, 1911).

The diagnosis in these cases rests upon: first, a consideration of the history. Important points for consideration are the age of the patient, exposure to pregnancy and the presumptive signs and symptoms, a history indicative of an antecedent tubal inflammation, a previous period of sterility usually of some years. This last point has been observed by all students of the condition and Parry remarks on what he calls "the previous inaptitude for conception" of these patients.

Amenorrhea of shorter or longer duration is a fairly constant feature and is followed in the majority of instances by irregular bleeding from the uterus, sometimes profuse, sometimes a mere staining. The history of passing bits of tissue or the demonstration of decidua in the discharge is important.

Pain if felt before rupture consists frequently in vague uneasy sensations in the pelvis. Sometimes it is more severe, colicky in type and accompanied by nausea.

In cases which show any of these suspicious symptoms an internal examination should not be neglected. The demonstration of a pelvic mass lying outside of the uterus, in the presence of a probable pregnancy, is a very suspicious circumstance. If this mass should correspond in size

with the duration of pregnancy, if it should be located in the course of the tube, if it be movable, moderately soft and very tender, we may fairly conclude we are dealing with a case of extra-uterine pregnancy. It must be remembered that it is sometimes easy to mistake a retroflexed pregnant uterus for an extra-uterine pregnancy.

> Review of 36 cases simulating tubal pregnancy. The following conditions may be mistaken for the latter: 1, an acute exacerbation of a dormant gonorrheal pyosalpinx; 2, sudden extension of a uterine gonorrhea to the tubes and peritoneum; 3, an early abortion if associated with salpingitis or a tumor; 4, an irregularly softened, misplaced, hyperesthetic uterus associated with tubal enlargement; 5, an unsuspected tumor associated with symptoms of early pregnancy; 6, ovarian hemorrhage or tubal hemorrhage from other conditions; 7, sudden and rapidly progressive salpingitis, appendicitis, and gastrointestinal perforations. Crossen (Jour. Amer. Med. Assoc., Feb. 12, 1910).

Often before a diagnosis *can* be made, usually before the diagnosis *is* made rupture of the tube or extensive separation and hemorrhage from the placental site supervenes. It was formerly thought that rupture was the most common outcome of tubal pregnancy. More careful examination of the specimens, however, has shown us that in many cases of supposed rupture we are dealing with a case of tubal abortion with hemorrhage from the site of implantation. Moreover, hemorrhage from this source, while less violent as a rule than in rupture, may be very severe and even fatal. Frequently, however, it is comparatively slow and by slow leakage is responsible for the majority of hematoceles which we find. Recent statistics indicate that these tubal abortions occur more frequently than does rupture. The tragic stage, however, may follow either process.

[The idea that rupture is not so frequent as has been supposed and therefore an extra-uterine pregnancy is not so dangerous a condition is fallacious. It is a matter of common knowledge that tubal abortion may give rise to a condition as serious as any of the accidents of ectopic pregnancy. I should not feel it necessary to insist on this fact were it not for an impression which is going abroad in regard to treatment, which I shall consider later. JOHN B. DEAVER.]

> A positive diagnosis before a rupture has been rare, but there are many instances in which a strong presumptive diagnosis should have been made and for lack of which the patient suffers. Most cases, however, do not come under the physician's notice until rupture, the symptoms being not much different from those of normal pregnancy. There is usually a cessation of menstruation for one or more periods, and in this case, with rupture threatening, it is usually re-established, irregular as to time, and of a tarry, sticky character which, according to some observers, is pathognomonic. The pain is usually cramp-like, occurring at intervals for several days, and following it there is a dark, sanguineous discharge, probably due to a partial rupture of the gestation sac. Microscopic examination will reveal traces of decidua in most cases. While the history of the case is important, a careful and thorough examination is advisable and great care should be employed to avoid rupturing the sac. The rupture in the doctor's office is a frightful accident—one which greatly involves his responsibility. L. G. Bowers (Jour. Amer. Med. Assoc., Feb. 12, 1910).

Rupture is the most serious accident of ectopic gestation. It may take place very early and be the first symptom. Cases have been reported of rupture in the first or second weeks of pregnancy. Usually it occurs in the second or third months, but occa-

sionally may be delayed into the later months. Secondary rupture may occur at any time after primary rupture up to term. Rupture is usually ushered in by severe lancinating pain in the hypogastrium, accompanied by shock, sometimes by syncope and frequently by nausea or vomiting. Following this the symptoms of internal hemorrhages make their appearance. Increasing pallor, rapid and weak pulse, sighing and labored respiration and air hunger, dimming of vision, with increasing but slight distention of the abdomen, signs of fluid in the flanks, general abdominal tenderness most marked in the hypogastrium and a peculiar doughy feel of the abdomen which is readily distinguished from the usual rigidity of inflammation of the peritoneum.

There are the symptoms of rupture and of hemorrhage *per se*. They are not always so frank and outspoken and in order to be sure of our ground it is frequently necessary to bring to our aid the history and the internal examination. In this condition as in so many others, the classical picture *in toto* is rarely seen and it has happened, paradoxically enough, as Douglas remarks, that many more diagnoses are made nowadays since the integrity of all the classical symptoms have been repeatedly attacked than when a clear average picture had

Differential Diagnosis between Extra-uterine Pregnancy and Early Abortion Based on a Careful Study of 28 Cases.

Extra-uterine Pregnancy.	Early Abortion in Uterine Pregnancy.
1. Advent is sudden.	Rarely sudden.
2. Pain is severe very early.	Not severe early.
3. Blanching of the face early.	Blanching of the face late, if ever.
4. Pulse very feeble and rapid early.	Pulse strong and full until late.
5. Hemorrhage usually not severe, but persists, even after the uterus has been thoroughly emptied.	Hemorrhage usually severe early and markedly, diminishes after the uterus is emptied and ceases entirely in a few days.
6. At first there is no elevation of temperature, and later it is rarely above 101° F.	Frequently, especially if there is sepsis, the temperature is very much elevated.
7. At one side of the uterus there is usually a very tender tumor, which is, as a rule, movable.	There is no tumor unless there is infection, and then it is rarely movable.
8. Boggy feeling behind the uterus.	Not present.
9. Usually the cervix is very slightly open.	It is open, especially if part of the products of conception are still in the uterus.
10. Shreds, decidual membrane and blood only escape.	An embryo may be found; if not, the microscope will show chorionic villi.
11. Late there will be marked diminution of the hemoglobin (30 per cent. to 70 per cent.).	No marked diminution of hemoglobin.
12. Rarely, if ever, polynuclear leucocytes.	Frequently present, especially if there is infection.
13. If the *cul-de-sac* of Douglas is opened, blood will escape with possibly an embryo.	No blood will escape.

Ralph Waldo (Archives of Diag., Oct., 1908).

been drawn and accepted. It will do then to know that the three cardinal symptoms are pain, menstrual irregularities and tumor if we appreciate their variability.

Conclusions based on a study of 214 cases: 1. Irregular flowing seems to play the important part given it in the books as a symptom of extra-uterine pregnancy. 2. The importance of a long period of sterility as a cause of extra-uterine pregnancy does not seem to be borne out by these statistics. 3. Conditions possibly leading to extra-uterine pregnancy: The fact that cystic ovaries, disease of the opposite tube, adhesions, or a previous miscarriage occurred in over 83 per cent. of 202 cases is suggestive, and is in agreement with authorities as to the possible relation of such conditions to extra-uterine pregnancy. 4. The fact that in only 26.5 per cent. of 207 cases the pain was sudden is of interest. In about three-fourths of the cases the sudden severe pain was preceded by pain of less severity, coming on gradually. 5. Of considerable interest is the leucocytosis observed in the cases in shock. This is apparently a perfect example of leucocytosis after hemorrhage. The finding of a temperature of 100° or over in 43.4 per cent. of the cases, and of a temperature of 101° or over in 14.4 per cent. of cases, is also of interest. Ordinarily it is supposed these cases rarely have any fever. Coues (Boston Med. and Surg. Jour., May 11, 1911).

[The question of great and timely interest in connection with the treatment of extra-uterine pregnancy has to do with the management of the case at the time of rupture, with associated hemorrhage and shock. Thanks to the early operation these complications are rare nowadays, but I fear, if the advocates of delayed treatment secure a following in the profession, that these cases may occur more frequently, and that cases which would be noted in the statistics of extreme conservatives as cures will later succumb to a condition which is the direct result of the Fabian policy. JOHN B. DEAVER.]

COMPLICATIONS.—I have already pointed out that spontaneous cures may occur without leaving a dangerous condition behind and have remarked on the rarity of such a favorable outcome. More usual is it for a collection of blood, often very large, to be left as a foreign body in the peritoneum.

These collections or hematoceles excite a reactive peritonitis which serves to glue together the intestines and encapsulate the mass of clots. Absorption and organization of such a clot may take place, but is usually very slow. In the mean time not infrequently infection occurs. The danger of this is apparent when we realize that an hematocele is nothing but a most inviting medium for bacterial growth, situated about the rectum or lower bowel, which harbors the most virulent bacteria.

[An infected hematocele is a serious condition and demands prompt evacuation and drainage. This is best done by way of the vagina, if possible. At times it is necessary to attack it by the abdominal route, accepting the danger of a subsequent peritonitis. JOHN B. DEAVER.]

Obstruction of the bowel is mentioned by Parry as the cause of death in a number of instances. The mechanism of this is by the peritoneal adhesions set up by the old extravasation of blood or a degenerated fetus in neglected cases.

Case of extra-uterine gestation sac which ruptured into the large intestine. A five-months fetus with cord and placenta was passed from the rectum, and the patient recovered. Martin (Münch. med. Woch., Aug. 21, 1906).

A pregnancy which is allowed after rupture to develop free in the abdomen or in the broad ligament later furnishes a very difficult problem to

the surgeon owing to the danger in dealing with the placental site, and the mortality in such cases is much higher than in the early cases. Left entirely to itself the fetus often becomes infected, and the earliest records we have of extra-uterine pregnancies are of cases in which this occurred, the resulting abscess later spontaneously discharging through the abdominal walls, when its nature was surmised by the appearance of degenerated fetal parts in the discharge. Sepsis, exhaustion and death were noted in 54 of Parry's cases.

Case of ruptured ectopic pregnancy which presented the combination of a ruptured ectopic pregnancy in which the following points of interest were noted: 1. Recovery following a ruptured ectopic gestation with a streptococcus infection of the sac and the peritoneal cavity, with a patient so alarmingly ill. 2. The presence of the indurated mass in the right quadrant of the abdomen which suggested an inflammatory condition, although in consequence of the finding of the streptococcus in the *cul-de-sac* and the cavity of the uterus an abdominal section seemed to be inadvisable at the time of the first operation. 3. The finding of streptococci in the fluid aspirated from the abdominal mass, showing that the peritonitis was spreading and calling for an immediate abdominal operation. Hunter Robb (Cleveland Med. Jour., April, 1911).

ETIOLOGY AND PATHOGENESIS.—In attempting to get a clear idea concerning the causation of extra-uterine pregnancy, one is quite awed and overcome by the vast number of hypotheses which have been advanced to account for this curious anomaly.

[It reminds us of the wealth of therapeutic suggestions with which we are favored in the case of diseases as yet resistant to all modes of treatment. It is not surprising that there is still considerable obscurity in the etiology. A correct understanding of the pathology of any condition presupposes a fairly exact knowledge of the normal physiology of the parts. There still exist many problems connected with maturation, ovulation, impregnation, implantation and development. Some of these problems carry us well back into the shadowy realms of the beginnings of life itself, that ultima Thule of the biologist.

The incompleteness of our information concerning these abstruse secrets of nature forces us here, as in so many other medical problems, to resort to the methods of induction and experience, and if we have not yet arrived at the point where we may safely take the inductive hazard it is because we may not yet have appreciated fully the saying of old Ambroise Paré that "such matters cannot be determined by sitting down and thinking, but by hard unremitting toil."

Gradually, however, our knowledge of the normal functions of procreation has been expanding and a sufficient number of cases have been observed, recorded and analyzed to enable us to recognize certain factors which evidently play an important part in the etiology. JOHN B. DEAVER.]

Lawson Tait originally thought that the ciliary current of the mucous membrane of the tubes and that of the uterus was in opposite directions, that of the tubes being directed toward the uterus and that of the uterus moving upward, thus forming a natural meeting place of sperm and ovum at the fundus. He considered it abnormal for spermatozoa to gain an entrance into the tubes and held that impregnation occurring in the tubes through this accidental invasion of the spermatozoön was very likely to give rise to tubal pregnancy. This beautifully simple conception has yielded to the iconoclastic power of observed facts. We now know that the ciliary current of the uterus as well as that in the tubes is downward. We know that the spermatozoa can

readily stem this current, their rate of speed being calculated by Henle as 1 cm. in three minutes.

We know that they quite regularly obtain entrance into the tubes and swarm up its lumen and it seems quite probable, if not certain, that impregnation in the tube is common, if not the regular method. Once fertilization has taken place development begins at once. The ovum, comparable in many respects to a parasite, rapidly throws out the chorionic villi which lay hold on the maternal tissues and by erosion secure anchorage and open up the intervillous blood spaces. Just how soon the ovum displays these grasping tendencies is unknown. The youngest ovum of which we know was discovered by Peters in the uterus of a woman who committed suicide three days after missing her period. It measured .6 x .8 x 1.3 millimeters and was firmly implanted with numerous projecting villi in the process of formation. Certainly this ovum was less than a week old. Just what condition must be met by the maternal tissues to permit of implantation is uncertain. Webster is quite certain that there must be a decidual reaction and a number of observers have reported having seen decidual formation in the tubes.

Normally the oösperm is swept down into the uterus before it effects a lodgment. The forces which accomplish this movement are the peristalsis of the tube and the action of the cilia. Whatever delays the ovum in transit, permitting it to put out the anchoring villi, in the presence of a suitable soil, renders imminent the occurrence of an extra-uterine gestation.

Forty-one cases of bilateral tubal pregnancy found on record to which the writers add a case in which there was a twin pregnancy in one tube and a simultaneous single pregnancy in the other. The size of the three 3-months fetuses proved that the pregnancies were practically simultaneous. In only 15 cases on record was the tubal pregnancy simultaneous on both sides. P. Launay and Seguinot (Revue de Chirurgie, April, 1911).

As to the nature of the soil required by the ovum we are not so certain. Concerning the influence of delay which is governed by mechanical causes everyone is agreed.

These causes may be classified as:—

1. Malformation: as diverticula, accessory ostia, and persistence of the greatly convoluted fetal contour of the tubes.

2. Obstruction from within: as in tubal polypi and torsion of the tube.

3. Obstruction from without: as in myoma and peritoneal bands and adhesions.

4. Inflammation, which acts by destroying the motor power of cilia and musculature and secondarily by the formation of different types of obstruction.

5. Excessive size of the ovum itself, as in the delay which occurs in external migration of the ovum.

The importance of the inflammatory factor in the etiology of ectopic gestation is becoming more and more appreciated and is even of use in the diagnosis, a history indicating more or less pronounced salpingitis tending to arouse our suspicions of the greater possibility of an extra-uterine pregnancy in a doubtful case.

An analysis of 170 cases in the author's clinic showed that tubal pregnancy sometimes results from an infan-

tile condition of spiral torsion of the tubes, but chiefly from residues of old gonorrheal or inflammatory puerperal processes. In the diagnosis inflammatory conditions may be differentiated from ectopic gestation by the leucocyte count and by puncture of the posterior vaginal wall. Fehling (Arch. f. Gynäk., Bd. 92, Hft. 1, 1911).

According to the site of implantation we recognize several varieties:—

1. The interstitial, located in that part of the tube which pierces the uterine wall.
2. The isthmial.
3. The ampullar.
4. The infundibular.
5. The ovarian.

These are the primary forms. Later the gestation sac by reason of rupture or growth may change its position, giving rise to the secondary forms.

Thus the interstitial form may be converted into an intra-uterine by rupture into the cavity of the uterus, into an abdominal by rupture into the general cavity or into an intraligamentary by escape between the layers of the broad ligament. The isthmial and ampullar forms similarly may become tuboabdominal, tubo-ovarian, abdominal or intraligamentary. An infundibular or ovarian pregnancy always tends to become abdominal. The last-named condition is one of the greatest curiosities of abdominal pathology. All the undoubted cases of ovarian pregnancy so far observed can be numbered on the fingers. The interstitial and infundibular forms are almost as great rarities; so that for practical purposes we have to do only with cases primarily isthmial or ampullar, of which the latter are most numerous, and with the forms secondary to these primary varieties.

Case of extra-uterine pregnancy in which the fetus was discharged by the rectum. Notwithstanding a pelvic abscess, an intestinovaginal fistula, general adhesive peritonitis, and phlebitis of both legs, the case ended in recovery. J. R. Laughlin (Jour. Amer. Med. Assoc., May 21, 1910).

Extra-uterine pregnancy assumes pathological significance when it undergoes ectopic attachment. The tubal ovum has a parasitic action, malignant in that it destroys maternal tissues; it embeds itself in the tube wall, and tends to the death of the mother. The growth of the ovum or the enlargement of the dead ovum mass, thinning and destroying the tube wall, leads to almost certain rupture of the tube. Primary rupture may be partial or complete and fatal. If incomplete, subsequent ruptures will be almost certain to follow. With rupture free hemorrhage occurs, which may prove fatal. There may be one rapid fatal hemorrhage or a series of minor hemorrhages. If death does not occur from hemorrhage, the blood and the ovum in the abdominal cavity may act as imitating foreign substances which lead to loss of function and pathological changes in the viscera, to local or general infection, thrombosis, embolism, etc. The dead ovum is almost as harmful as the living one, from the standpoint of rupture, and may be more harmful as a focus of infection. C. W. Barrett (Amer. Jour. of Obstet., June, 1911).

The natural outcome of extra-uterine pregnancy, as stated in the definition, is early interruption, whether by reasons of insufficient blood supply or unfavorable mechanical conditions for the continued development of the fetus.

The most common event is the formation of a tubal mole from the slow leakage of blood about the sac. This soon results in the death of the fetus and cessation of growth. In this way spontaneous recovery may

occur. I have several times in the course of pelvic operations encountered old tubal hematomata which were clearly the result of a previous tubal pregnancy which had terminated itself and retrogressed without giving the patient any great inconvenience. That this is not a frequent occurrence our clinical experience and the infrequency of such operative findings testify. There is evidence to show that even after the death of the fetus the chorionic villi may continue to grow and exert an erosive action on the wall of the tube which, coupled with the distention due to hemorrhage, may bring about a rupture. More common than this is the gradual extrusion of the mole from the fimbriated extremity, a process known as tubal abortion. Rupture of the tube and tubal abortion may take place rapidly without the previous formation of a mole. These are apt to be the fulminating cases.

Hemorrhage is more free in case of rupture than in abortion as a rule: more free in rupture into the general abdominal cavity than in rupture into the broad ligament, more free when the site of rupture involves the placental attachment, and more free at the cornual end of the tube than at the ampullar end.

[This latter tendency was tersely expressed by Formad, who used to say, "Ruptured cornual cases belong to the coroner; ruptured ampullar to the surgeon." Surgery in its march has modified this statement, but it still serves to point out the relative dangers. JOHN B. DEAVER.]

Hemorrhage is the outcome of extra-uterine pregnancy which chiefly concerns us from a practical standpoint. It is probable that no case of ectopic gestation occurs which is not accompanied by hemorrhage at some time. It may, however, be early or late, slow or rapid, slight in amount or profuse. It is the chief, though not the only, factor in the production of so-called shock, and is the main agent in a fatal outcome. I shall have more to say concerning hemorrhage under the question of treatment.

If the patient be fortunate enough to survive the primary rupture and the fetus live, she still has to face the possibility of a second rupture of the gestation sac in its new position. Occasionally an extra-uterine pregnancy may progress to term. Usually this is rendered possible by the escape of the fetus within its amniotic sac into the general abdominal cavity, the placenta remaining attached at the primary site. In this event, after a spurious labor at term, the fetus dies and offers an inviting site for infection.

[Operation is here indicated on the same principle as in the case of any foreign body which threatens the host. This holds true in spite of the well-known fact that in some instances the fetus has caused little harm, being converted into a lithopedion or adipocere. Such a late terminal event presupposes a series of diagnostic failures which we trust, now that the condition is so well known and understood, may not come to pass. JOHN B. DEAVER.]

TREATMENT.—This involves a discussion of the immediate considerations concerning an active *versus* expectant mode of treatment in cases of rupture.

[It has long been my practice to operate every acute case of extra-uterine pregnancy without delay and my results have been so uniformly good that it would never have occurred to me to reopen the question. Robb, in 1907, came forward with the as-

sertion that surgeons were losing many of their desperate cases from overhaste in operating during shock. He believes that shock is mainly due to the effect of the accident of rupture upon the nervous system, that it would be a great rarity for a patient to bleed to death and that cases in which the loss of blood in itself would be sufficient to bring about a fatal termination would seldom be seen in time to save the patient. He bolsters his position by animal experiments, having observed that dogs do not die of hemorrhage even after section of the uterine and ovarian vessels.

Just what he considers the cause of death in these cases is not clear. The coroner's statistics of Dr. Formad, though he admits that it is on record that in certain instances the amount of blood which was found was enough to fill the abdominal cavity, Robb dismisses by saying that "such statements are entirely too meager to give us any definite knowledge, nor can they be entirely depended on." He also says in this regard that "in a given fatal case it must also be proven that there were no other and possibly equally important factors in the causation of the fatal result." He not only doubts that the coroner saw the blood, but he invites us to prove that the patient did not die of cerebral apoplexy instead of abdominal hemorrhage. As for the animal experiments I can only say that, if he has not seen a woman die from hemorrhage from a uterine artery, he has been more fortunate than I have been, and that I therefore still resort to the old-fashioned expedient of tying as secure a knot about that vessel as I am able. JOHN B. DEAVER.]

Formerly it was not such an uncommon thing for these patients to bleed to death. Of the 500 cases reported by Parry there were 336 deaths, 174 of which were from rupture and hemorrhage. Of 113 of these in which the time of death was stated 81 had died at the end of 24 hours and at the end of 48 hours only 15 were left alive.

Of course this gives a greatly exaggerated idea of the danger because in those days only the evident and severe cases were noted. Still it serves to show that, without operation, death, which was shown by autopsy to be associated with excessive hemorrhage, was not so uncommon a sequel. If these deaths were not due to hemorrhage, what did cause them?

[Has anyone seen a death from shock of rupture with an insignificant or even a moderate amount of blood in the peritoneal cavity? In the cases which I have seen in this so-called state of shock, the condition of the patient bore a striking parallelism with the amount of blood found in the abdominal cavity. I wish to enter a strong protest against the loose use of the term shock in this condition as well as the vicious tendency of such flashy phrases as "adding shock to shock. JOHN B. DEAVER.]

The great danger in these cases is not from the shock of rupture, but from the subsequent hemorrhage. Or, to be very conservative, severe hemorrhage is necessary to produce the fatal outcome. Let us consider for a moment this factor, shock. It is known that any acute lesion of the peritoneum produces, through shock to the great abdominal nerve centers, a certain train of symptoms, whether the lesion be due to rupture of the appendix, twisted pedicle of an ovarian tumor, passage of gall-stones, acute strangulation of the intestine, or rupture of an extra-uterine pregnancy, and to this train of symptoms Gübler has given the name "peritonism." These symptoms are independent of inflammation or of septic intoxication. They are: pain, profound exhaustion, distressful anxiety, pallor; soft, quick pulse; cold extremities, shallow respiration, nausea and vomiting. These vary in degree and are common in some degree to all cases in which there has been a wide

and abrupt impression upon the nerve centers of the abdomen. This is the train of symptoms which follow immediately upon an acute rupture of the gestation sac and gives the picture properly denominated as shock. This shock as such is practically never fatal. Clinical evidence is conclusive on this point. We do not find our patients dropping over dead from acute strangulation, twisted pedicles or tubal ruptures. The shock exerts its maximum influence at the moment of the tearing injury to the peritoneum and sympathetic trunks and practically ceases at once with the release of tension after the laceration has been effected. This factor is sudden, momentary, expends its energy and ceases. Reaction begins, or would begin at once, either spontaneously or with the aid of stimulants. This sudden insult to the peritoneum and the great sympathetic centers is not what places the patient's life in jeopardy and holds her hovering in the balance for hours.

This is but the advance agent of the real executioner, hemorrhage. Read in the same order as before, leaving off the pain in the beginning, we have in the symptoms of shock the symptomatology of hemorrhage: Profound exhaustion, distressful anxiety, pallor; soft, quick pulse; cold extremities, shallow respiration, air hunger, nausea and vomiting.

[Who is that man who will tell us in these cases where shock leaves off and hemorrhage begins to play the leading rôle? I feel most strongly that we are dealing here with a wrong use of words, that there is a sophistical "nigger in the woodpile." I do not believe that the patients reported by the advocates of the expectant treatment as suffering from shock were suffering from primary shock, but instead from shock plus hemorrhage, and that, by the time they were seen by the surgeon, that hemorrhage was playing by far the chief rôle. Those patients who are fortunate enough to lose but a small quantity of blood at the time of rupture react from the shock with considerable promptitude. By the time proper surgical intervention can be brought to bear, their condition is such as to give the surgeon little immediate anxiety as far as the shock of operation is concerned. These patients should be operated at once on account of the danger of secondary rupture or a renewal of bleeding. They should all get well. JOHN B. DEAVER.]

An immediate operation detracts nothing from the chances, but guards against imminent danger. Those patients who, when seen an hour or several hours after rupture (I am speaking of conditions as we find them, for patients do not come to a hospital or doctor's office to be handy at the time of rupture), are hanging in the balance with the symptoms some are pleased to call shock are not suffering from shock, but rather of shock plus hemorrhage, shock in small type, hemorrhage in large red capitals, and the examples of reaction are not proofs of the wisdom of waiting, but of the fact that many desperate cases will stop just short of bleeding to death if left to themselves, a fact which has for years been patent to all.

> The necessity for surgical interference lies in the fact that one can never foretell the result if a case is left to nature. Tubal abortion usually occurs before the sixth week of impregnation, pregnancy being usually arrested thereby. H. C. Coe (Annals of Gynec. and Ped., Jan., 1906).

There are certain factors which would favor the cessation of bleeding, such as a long and voluminous sigmoid or omentum wedging down in the pelvis, but, as we are not often

furnished with a diagram of interior arrangements in these cases, we do not know whether these stanch allies are on the ground. The character of the rent and the coagulability of the blood we cannot estimate.

[As sure as there are immutable laws of hydrostatics and of the circulation of the blood, these patients have died in the past in considerable numbers from hemorrhage and occasionally die today from that cause, and the only reason more do not die of it is because of the early operation practised by clinical surgeons.

I am willing to grant that a patient should not have a "penknife" operation done on her before she has recovered from her first faint. There is reason in all things. It is equally true that a patient in *articulo mortis* should not be subjected to operation. "The resources of surgery are rarely successful when practised on the dying. These principles, however, should not be made use of to attack a mode of treatment which has been crowned with the highest success. JOHN B. DEAVER.]

> The quicker a woman with ectopic gestation is operated upon, the better are her chances for recovery. Furthermore with few exceptions, the operations should be done by the abdominal route, and the element of time be considered as important. A quick operator's patients have a better chance than have those of a slow operator. A careful peritoneal toilet is not desirable; remove the large blood-clots that are readily accessible and close the abdomen without drainage. H. J. Boldt (Mo. Cyclo., April, 1908).
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> The pathology of the condition shows that treatment directed toward the killing of the ovum is irrational. Patients in good condition, with or without rupture, are almost certain to have future trouble, and should be operated upon as soon as possible. Patients in bad condition, with concealed hemorrhage, show collapse according to the loss of blood, and rational treatment should aim to stop further hemorrhage. Opening the abdomen and ligating the proper vessels is the only way to effectively control internal hemorrhage, and when done rapidly and carefully does not tax the patient severely. Universal clinical experience and study of the pathology of this condition show the danger of delay. While the patient is living, the more desperate the case, the greater the need of immediate action. C. W. Barrett (Amer. Jour. of Obstet., June, 1911).

My position then is this: A continuance of the collapsed condition, commonly, and as I believe erroneously, termed shock, for a longer time than one hour indicates that a considerable hemorrhage has occurred and may be continuing. The surgical indications are clear—stop the bleeding; stimulate. Let us not revert to the dark ages in the ranks of those who "watched the life ebb rapidly from the pale victim of this accident, but never raised a hand to help her."

> According to Schauta, the maternal mortality in non-operative cases is 68.8 per cent. The writer is inclined to feel that this percentage is too high, that more cases of ectopic gestation escape recognition and live than we have suspected. At the Columbus Hospital operation is always resorted to, and, performed speedily and promptly, should not give a mortality of over 2 per cent. The dangers are from shock, hemorrhage, sepsis, exhaustion, and intestinal obstruction. J. M. Keyes (N. Y. Med. Jour., Aug. 6, 1910).

Since 1900 I have had 110 cases of extra-uterine pregnancy, many of them of the acute type, without a death.

My procedure in these urgent cases is as follows: If the condition be very low, stimulation is begun on admission by **hypodermoclysis** and **strychnine**. If there is extreme restlessness, **morphine** is a valuable adjunct.

They are placed on the table with as little disturbance as possible and a light quick etherization given. Preparation is rapidly completed and intravenous transfusion of **normal saline solution** started as the abdominal incision is made. "Get in quickly, get out quicker" applies here as forcibly as anywhere in surgery. The offending tube and ovary are removed. The clots are scooped out, and, if the condition of the patient warrants, the abdomen is flushed out and filled with normal saline before closure.

> In 70 cases of extra-uterine pregnancy encountered by the writer the fetus was found behind the uterus eight times, four times in the tube, in 1 partly in the tube and partly in a sac, in 2 in a small sac near the tube, once in a cavity formed by the tube and ovary, once on top of the bladder, and once on top of the uterus. In 13 it was found in the lower part of the abdominal cavity. In two instances the fetal structures were apparently safely implanted among loops of intestine. In one of these a living 4-months fetus was found. In this instance the history did not clearly determine the date of expulsion from the ruptured tube. The routes employed for operation in his series were the abdominal fifty times, the vaginal nine, and the vaginal immediately followed by the abdominal or *vice versâ* eleven times. Bovee (Amer. Jour. of Obstet., April, 1910).

I have frequently seen the patient go off the table with a far stronger pulse and in better condition than before the operation, a sufficient refutation of the charge of "adding shock to shock." I have rather refused to allow hemorrhage to be added to hemorrhage, and now I am not afraid to fill her vessels with sufficient fluid to satisfy the mechanical needs of the circulation.

[My last case before this article was written happened to be most appropriate to this discussion: A young woman, aged 24, married three years, with nothing of note in her past history. She had had one child nine months ago, which died in January. No miscarriages. Menstruation had always been regular and normal up to her January period, which she missed. At the February period she bled quite profusely and for a longer time than usual. No staining since.

Suddenly at 6 A.M. on February 12th, during coitus, she had an acute pain in the lower left side of the abdomen, followed in a few minutes by syncope. Soon she recovered, but fainted several times in the course of the morning, and vomited several times. Gradually grew weaker and grew short of breath. On examination she did not have a particle of color in her skin or lips. Expression was anxious: she was restless and dyspneic. The pulse was about 180 and barely perceptible. Her abdomen was moderately distended and tender in left side low down. Vaginal examination was negative except for tenderness in the left lateral fornix.

She was taken to the operating room and subcutaneous infusion started with the ether. Preparation having been quickly accomplished, the operation and intravenous transfusion were started together. A left-sided tubal pregnancy (see colored plate) the size of a hickory nut was found in the isthmial portion about 2 cm. from the cornual extremity. Through the tube was a perforation only about as large as a pinhead. No time was wasted in determining whether there was any active bleeding. Tube and ovary were removed. As the patient's condition was improving on the table, I washed out the blood, of which there was a large quantity, and filled the abdomen before closure with salt solution.

Her pulse, which before the operation was 180, at the end of the operation was 140 and much improved in quality. She was put back in bed and continuous proctoclysis started. JOHN B. DEAVER.]

I wish to call attention to the value or rather necessity of filling the empty blood-vessels with saline in these depleted cases. In the above case, the amounts used were as follows: By hypodermoclysis at the

Tubal Pregnancy. (*J. B. Deaver.*)

beginning, 1000 c.c. Intravenous transfusion during the operation 2000 c.c. Left in the abdomen at least 1500 c.c. Then in the twelve hours after operation her thirsty vessels absorbed by way of the large bowel 4000 c.c. additional. Nearly nine liters of saline, over two gallons of fluid to meet the mechanical needs of the circulation. Without this saline my patient would have run grave danger of dying on the table. As the intra-abdominal pressure is released by incision the blood flows into the "splanchnic tank" and from the great depletion due to hemorrhage nothing is left in the great vessels for the heart to pump. The medullary vessels are asphyxiated and death results. This restoration of the fluid volume of the blood is a most important point and will eliminate what is I suspect, the most potent factor in that additional shock so feared by the misguided advocates of expectancy.

It is now universally agreed that during active hemorrhage consequent on tubal rupture or abortion the correct treatment is to open the abdomen and remove the gestation sac. In the writer's series of cases this was done in 16. In 2 of these the patients when seen were collapsed and almost pulseless. Their condition warranted only slight anesthesia, and after removing the ruptured tube the abdomen was closed without any attempt to clear out the blood-clot which filled the abdomen. From the writer's experience in these cases immediate operation, even in the collapsed condition of the patient, is better than temporizing with saline infusion in the hope of improving the condition of the pulse before operating. The best way to improve the pulse is first to open the abdomen and remove the source of bleeding, and then administer salines. In 14 cases so treated the condition of the patient permitted of the delay necessary for preparatory treatment and for the removal of all blood-clots from the abdomen. Kynoch (Lancet, June 10, 1911).

JOHN B. DEAVER,
Philadelphia.

ABSCESS.—DEFINITION.—A circumscribed collection of pus in an adventitious cavity, the result of localized inflammation due to infection by pus-forming microbes, differing from *diffuse suppuration* which is not circumscribed and from *purulent effusion* or *empyema* which is found in a natural or pre-existing cavity, as the pleura, pericardium, mastoid cells, etc.

VARIETIES.—An abscess may be *acute,* or *warm,* when due to pus-microbes only: staphylococci, streptococci, and others; *chronic,* or *cold,* when due to a specific microbe, especially that of tuberculosis.

Abscesses have been classified according to:—

1. **Etiology.** — Atheromatous, embolic, fecal (stercoraceous), metastatic, miliary, ossifluent, puerperal, pyemic, residual, symptomatic or congestive, tropical, tubercular (strumous, lymphatic, or scrofulous), etc..

2. **Pathology.** — Acute or warm, canalicular, caseous, chronic or cold, critical, gangrenous (anthrax), ligneous, perforating, phlegmonous, etc.

3. **Location (Organ or Tissue Involved).**—Alveolar (gum, jaw, teeth), of axilla, bone (subperiosteal), brain (cerebral, cerebellar), bursal, corneal (hypopyon), deep, dorsal, follicular, hepatic, of hip-joint, iliac, ischiorectal, lacunar, lumbar, mammary (milk, weid or weed, breast), marginal, mediastinal, meningeal (extradural, subdural), of neck, nephritic and perinephritic, of nose, of palate, palmar, of pancreas, perityphlitic, popliteal, of prostate, psoas, rectal, retropharyngeal, of skin

(furunculosis), of scalp, of space of Retzius (properitoneal cavity), spinal or vertebral, of spleen, superficial, thecal, urethral and periurethral, vulvo-vaginal (Bartholinian), etc. All the above varieties will be considered under their respective anatomical heads.

ACUTE, OR WARM.—Symptoms.—An acute abscess may be either superficial or deep. When it is superficial the local symptoms predominate; when it is deep the general symptoms are more marked.

The pain, due to compression of the nerves by the disturbed tissues, varies in degree with the density of the parts involved, the local supply of sensitive nerves, and the tension produced by the inflammatory products. In superficial abscess the pain is generally localized in the center of the swelling, and is sharp and lancinating; in deep abscess it is more diffuse and dull.

Redness is due to engorgement of the local blood-supply, and the swelling to the inordinate distention of the vessels and the secondary escape of blood-plasma, colorless corpuscles, etc., into surrounding tissues. It may become very great in certain regions, such as the lids, the lips, etc., in which the cellular tissue is lax. As the purulent foci run together and form a single cavity, the center of the tumefaction becomes soft, and darker in color, and the abscess is said to be "pointing."

Edematous infiltration in superficial abscess denotes the presence of pus; in deep abscess subcellular edematous infiltration is an important sign of deep suppuration.

Local heat, throbbing, and tension are mechanical results of the causes of tumefaction tending to decrease as the formation of pus progresses.

Hyperpyrexia is in relation with the location of the abscess, the ease with which the pus-microbes can enter the circulation, and the amount of pus and necrotic tissues present. In superficial abscess there is but little rise of temperature, but in deep abscesses it sometimes reaches 104° F. (40° C.) at the time the wall of granulation tissue is established. A remission of about one degree each morning usually takes place. When the pus has found an issue, or has become completely surrounded by the limiting membrane, the intensity of the fever is usually reduced.

In a superficial abscess, if a chill occur, it is usually very slight, and appears between the fourth and the eighth day. It indicates the formation of pus. In a deep abscess a chill generally occurs, lasting from a few moments to half an hour.

Fluctuation is generally obtained when the purulent focus has been formed. A sharp localized pain on pressure over the apex of the swelling obtained at this time supports the likelihood that pus is present, but fluctuation is liable to be a misleading symptom.

Interference with motion or the normal functions of a part is sometimes produced through the proximity of an abscess.

In deep-seated abscess any or all of the general symptoms of abscess may be lacking, except loss of flesh and strength. This is especially true of hepatic or cerebral abscess. The symptoms usually present are local tenderness and pain, pressure symptoms, overlying edema, brawniness, muscular rigidity and ankylosis of neighboring joints, in addition to the symptoms of acute suppuration—fever, chills, sweats, anorexia, restlessness, etc.

Etiology.—Inflammation due to traumatisms and lesions of all kinds, especially the introduction of foreign bodies under the epidermis, are the usual causes of abscess. While blows do not apparently produce superficial lesions in the majority of cases, the fact remains that an invisible abrasion may be present and serve as a channel for the introduction of the pyogenic organism. The cutaneous glands, through weakened local resistance, may also become the transmitting media. Any cause removing the epithelial layer of the mucous membrane may also form the primary etiological factor of an abscess in the membrane or in the submucous connective tissue. Abscesses also arise in connection with the various septic fevers.

The three essentials in the formation of an abscess are: pyogenic organisms in sufficient numbers and virulence, their proper implantation within the tissues, and a sufficiently low resisting power, either local or general.

Pathology.—While several varieties of micro-organisms are found in the pus of an acute abscess, the principal ones which ordinarily cause purulent inflammation are the *Staphylococcus pyogenes* (*aureus* and *albus*), *Streptococcus pyogenes, Micrococcus gonorrhœæ, Bacterium coli commune, Bacterium pyocyaneum, pneumococcus,* and the *Sarcina tetragena.* Less frequent in the production of suppuration are the typhoid bacillus, the influenza bacillus, the diphtheria bacillus, the actinomyces, etc.

> Suppuration can occur in man without the presence of bacteria. Both in animals and in man, suppuration may be due to the irritation of chemicals. Investigators have shown that suppuration is only a certain stage of inflammation, not a separate qualitative form of inflammation. The serous formation of blebs and bullæ becomes purulent without the presence of bacteria. Karl Kreibich (Wiener klin. Woch., June 13, 1901).
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> Case of subcutaneous abscesses due to the gonococcus in a child 2 years of age. The little patient developed an acute anterior urethritis and areas of induration to the left and right of the anus. All were found to contain pus in which gonococci were present. Gershel (Med. Record, Feb. 7, 1903).
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> Chronic suppurative processes are very frequently unattended by fever, while acute suppurative processes are frequently unattended by fever. In a given case, therefore, the absence of fever must have little weight by itself in excluding the possibility of suppuration. Since a rise of temperature above 100° F. occurs in about two-thirds of all aseptic cases, the presence of fever *alone* must have little weight in making a diagnosis of suppuration. Lyman Allen (Inter. Jour. of Surg., Feb., 1905).
>
> In the common acute type of glandular suppuration in infancy and early childhood suppuration is not diffuse, but more or less limited by the line of the distended capsule of the gland. The infection having been brought under control by the sacrifice of the parenchyma of the gland, nature seeks as speedily as possible to evacuate the pus and detritus. Therefore, in incising such abscesses a destructive process should not be checked by heroic measures, but the requisite amount of aid just given to complete a conservative process. Southworth (Archives of Pediatrics, Sept., 1911).

Suppuration is almost invariably preceded by inflammation due to the pyogenic micro-organisms. The first effect of the bacterial toxins on the local circulation is to cause an increased rapidity of the flow of blood in the part, the vessels becoming engorged and dilated. This is succeeded by slowing of the current and passage through the vascular walls and into the surrounding

tissues of colorless corpuscles (leucocytes), a few red corpuscles, and blood-plasma, the latter of which become coagulated and finally softened. One or several cavities are thus formed; but, if the cavities are multiple, the barriers usually soften and a single focus is established. The pus is composed of the corpuscles which perish in the cavity thus formed, the broken-down remains of tissue, and the plasma. At a distance from the location of the abscess the circulation is normal, but, as the diseased area is approached, the slowing of the blood-current becomes gradually more evident, until a zone of living leucocytes is met, forming a protective barrier around the abscess cavity. The surrounding parts also become permeated with new vessels, and a zone of granulation tissue (the pyogenic membrane of older writers) is formed. The spread of the suppuration being thus checked, the pus is forced to the surface because it finds the least resistance in that direction; but, if an aponeurosis or fascia interfere, it burrows until an exit is found.

The rôle of the white corpuscles (leucocytes) has been interpreted in various ways; Cohnheim considered them as elements of repair; others have attributed to them the rôle of scavengers. The accepted theory at present, however, is that of Metchnikoff, who considers them able to attack and destroy invading organisms. The process is termed by him *phagocytosis,* the cells being called phagocytes (φαγω, to eat, and κυτος, a cell).

The dead leucocytes in pus must be looked upon as the cells that have been brought up rapidly to interfere with the spread or diffusion of the products of the micro-organisms; a large number of these cells coming in contact with the poison in a concentrated form may succumb to its action; but before doing so they are able to deal with a certain quantity of the poisonous material, breaking it down and rendering it inert. Other cells are constantly being brought up to assist these, until, at length, the bacteria are completely hemmed in. They live for a short time on the dead tissues; but, being localized by the barrier of leucocytes, they ultimately die, either from inanition or because they are poisoned by their own products or by immunizing constituents of the blood-plasma. It is found very frequently on opening an abscess that no organisms can be seen, those that were originally present appearing to have undergone degenerative changes and to have been taken up by the phagocytes, or devouring cells.

The process includes, according to Sajous, participation of the proteolytic or peptonizing action of enzymes in the serum supplied in large quantities to the abscess. The prevailing view is that these are produced by the pyogenic bacteria. From his viewpoint (see "Internal Secretions," vol. ii, 4th ed., 1911, p. 907) these ferments are secreted (though originally derived from the pancreas, thyroid, and adrenals) by phagocytes (Metchnikoff's trypsic cytase), themselves and their liquefying action has for its purpose to destroy the bacteria and their toxins in the abscess. The pathogenic organisms are first sensitized and softened by opsonins and agglutinins (thyroid secretion), and thus rendered vulnerable not only to the digestive action of the phagocytes when ingested by these cells, but to the ferments (trypsin mainly) they contribute to the abscess fluids, in which they accumulate in large numbers.

Differential Diagnosis. — Fluctua-

tion only indicating the presence of fluid, the presence of this sign without the other symptoms mentioned should inspire great circumspection, especially if surgical measures are employed.

ANEURISM is the most dangerous condition to fear. It has, however, a less acute history, a peculiar thrill and expansile pulsation, and can only exist in close proximity to a large vessel.

Certain SEMISOLID GROWTHS may simulate an abscess. When the possibility of an aneurism has been eliminated, a fine trocar or exploring needle, if carefully used, will determine the diagnosis.

Prognosis.—This depends upon the general health of the patient. In the robust a suppurative process usually reaches the stage of resolution without giving rise to complications. In individuals weakened by disease, hereditary or acquired, an abscess may be protracted and exhaustive, and diffusion is more likely to occur if resisting tissues interfere with the superficial evacuation of the pus. Deep abscesses are especially prone to become protracted through this cause, the resistance of muscular aponeuroses, etc., forcing the pus into the cellular interstices. Fistulous tracts, or large suppurative areas, are thus created, and the patient may succumb to blood poisoning or asthenia.

Treatment. — *General Measures.*— Rest and elevation of the affected region, if possible; salines, if purgation is necessary. Easily assimilable food, but not low diet; avoidance of stimulating beverages, alcohol, coffee, etc.

Internal Remedies.—If the case is seen early the suppuration can sometimes be arrested by the use of one of the following agents, supplemented by one of the local applications: Tincture of **aconite**, 3 to 10 drops every hour, closely watching the patient's pulse; tincture of **veratrum viride**, 1 drop every hour until the pulse becomes slower, the skin moist, and slight nausea occurs; or **calcium sulphide** (sulphurated lime), $\frac{1}{10}$ grain every hour; or, again,

℞ *Sulphate of quinine*, 1 grain.
Ext. of nux vomica, ¼ grain.
For one pill, to be taken every three hours.

Many incipient abscesses disappear under the internal use of the **hypophosphites** of potassium, sodium, and calcium. They also act as an excellent prophylactic, if given before pus has formed. Tousey believes them to be more efficient than **calcium sulphide**. The combination used by Tousey is 5 grains of calcium hypophosphite, and 2 grains each of the sodium and potassium hypophosphites, administered in syrup or two capsules, followed by half a glassful of cold water.

Fresh **brewers' yeast** in doses of 5j to 5ij in water or undiluted, just before or during meals, is a favorite remedy with many, although diarrhea sometimes results, even when the yeast is fresh. A substitute preparation is made by macerating compressed yeast in water. Desiccated yeast is also used.

In addition to these internal remedies, we should not forget that stimulation, nutrition and general hygienic measures are of considerable value.

Thyroid gland in doses of 1 or 2 grains three times daily hastens the disappearance of abscesses, by increasing the proportion of opsonins in the blood (Sajous).

> **The authors report on the use of fresh normal blood-serum** from the horse or from cattle in the local treatment of acute suppurative processes in 100 cases. The pus was first aspirated, serum next injected to rinse out the cavity, using a needle closed at the end, but with a row of openings just above

it; then the excess of fluid aspirated, and the opening covered with a bit of sterile gauze held by adhesive. It is important that all the excess of serum be removed from the cavity; otherwise, symptoms of serum intoxication may follow. The serum apparently produces both a passive and an active immunity, stimulating leucocytosis and phagocytosis. Better healing can be obtained by this method, according to the authors, than in any other way. Acute abscesses in the soft parts, whatever be the micro-organism present, show especially good results. One treatment with the serum generally suffices. L. Fejes and E. Gergo (Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie, xxiii, 1911).

External Remedies.—The surface is carefully cleansed with **antiseptic soap** and sprayed with a 2 per cent. **carbolic acid solution,** or with **hydrogen peroxide,** every two hours, the atomizer being used for ten minutes at each sitting. (Verneuil.)

Compresses dipped in hot 1:4000 **corrosive sublimate solution** are very effective. If abscess is upon an extremity, a 1:4000 **corrosive sublimate solution** may be employed as a bath for the limb, the latter being left in the solution several hours at a time.

A solution of **nitrate of silver** (30 grains to the ounce) may be applied frequently with a camel's hair pencil.

Tincture of **iodine** may be applied in the same manner every three hours.

When the surface becomes very tender, **belladonna ointment** may be rubbed in every two hours.

In abscesses characterized by very severe pain a 10 per cent. solution of **cocaine** may be introduced **by cataphoresis,** the anode sponge of a galvanic battery being applied to the part. The sittings should last five minutes, and be repeated every three hours, the current not exceeding 5 milliampères. During the intervals **warm fomentations**—with borated, camphorated, or pure water—are of great value.

Encouraging results obtained in the treatment of tendon-sheath phlegmons and suppurating inflammation in general with **superheated air,** applied with an ordinary apparatus. It is used twice a day for two or three hours each time, maintaining a temperature of from 90° to 110° C. (194° to 230° F.) within the frame at half its height. Thus arranged, the temperature on the skin averaged 44° or 47° C. (111° or 116° F.), and the acceleration and sweating induced seemed to keep the temperature of the skin within due bounds. The applications of the hot air are made the day after the abscess has been incised and evacuated, and the cavity packed with iodoform gauze. He also states that neglected injuries of the fingers which would otherwise have necessitated amputation healed under this hot-air treatment without requiring operative measures, and recovery was hastened. This treatment also caused an abolition of pain. (Zentralblatt für Chir., Oct. 24, 1908.)

Pads of gauze wrung out of **hot boric acid solution** (an ounce to a quart of water), applied as hot as the patient can bear them, and well covered with oiled silk to keep in the heat and moisture, are the best; wherever applicable, as with the hands or feet, the inflamed part should preferably be submerged every hour for a period of five to ten minutes in the hot boric solution itself.

Wright's Bacterial Vaccines.—Treatment of staphylococcus and streptococcus infections (abscess, suppuration, etc.) by the therapeutic inoculation of staphylococcus and streptococcus vaccines, as suggested and developed by Sir A. E. Wright, of London, has found many endorsers. A bacterial vaccine is a sterilized, standardized emulsion of the infecting micro-organism. It is made by scraping the film of

a recent agar culture into a 1 per cent. salt solution, sterilizing at 60° C. (140° F.), and subsequently standardizing to a given number of micro-organisms per cubic centimeter. The method is, however, a new and complex one, and, until its use has been more thoroughly explored, it should only be employed under the guidance of an expert. Whether an opsonic control of the injections will always be necessary still remains to be shown, but in all cases the use of the vaccines should be preceded by a most careful bacteriological examination, and the particular vaccine should be prepared for each individual patient. The dose of staphylococcus vaccine is 100 to 1000 millions; an inoculation being made every ten days. The dose of streptococcus vaccine which is more toxic than staphylococcus is 20 to 60 millions; the inoculations being repeated weekly or every two or three weeks.

The writer has tried the **vaccine** treatment of staphylococcus affections in 20 cases and obtained encouraging results, especially for recurring furuncles. Jensen (Hospitalstidende, Mar. 3, 1909).

Wright's comparatively simple theory of opsonins and its practical application have been rendered needlessly confusing to the average practitioner. As Wright points out, the great causes of failure in previous tuberculin treatment was the giving of too large injections and too frequent repetition of the dose, causing a marked negative phase and keeping it up. The writer has had remarkable success in various types of staphylococcus infections; obstinate cases of acne and furunculosis, impetigo, palmar abscess, and in a very distressing case of what had been called psoriasis, but which he thinks was an extraordinary case of staphylococcic dermatitis, and which yielded rapidly to **opsonic treatment** with an autogenic culture of *Staphylococcus aureus*. A. P. Ohlmacher (Jour. Amer. Med. Assoc., Feb., 1907).

Case of furunculosis, subperiosteal abscess of the head, and necrosis of the bones of the skull treated by operation and **autogenous vaccine.** *Staphylococcus aureus* was recovered from the parietal abscess and from the blood. An autogenous vaccine was made, and 4 doses were given at intervals of four days. The first dose was 50,000 000, the second 100,000,000, and the last 2 150,000,000. With no constitutional reaction, the local condition rapidly improved. The general condition of the patient improved, but a portion of the bone at the base of the abscess was denuded and necrosed. At a later date this sequestrum was removed and the patient was given 3 more injections of the autogenous vaccine at four days' interval, each dose being 150,000,000. Within three weeks the patient was in normal condition. The author urges preference for the autogenous vaccine. G. G. Ross (Monthly Cyclo. and Med. Bull., Sept., 1910).

Bier's hyperemic treatment (passive congestion or artificial hyperemia) of acute abscesses has given excellent results as to immediate relief of pain and reduction of inflammation.

Inflammation, according to Bier, does not in itself represent a diseased condition, but is a phenomenon indicating the body's attempt to resist a deleterious invasion. To increase this beneficent inflammatory hyperemia resulting from the fight of the living body against invasion, is the aim of Bier's hyperemic treatment. The blood must, however, continue to circulate; there must never be a stasis of the blood. Bier's method artificially increases the redness, heat, and swelling, three of the four symptoms of acute inflammation. He discards all means that tend to subdue inflammation.

Bier produces this hyperemia by any

or all of three methods: Elastic bandage or band, cupping glasses, and hot air. In the use of the elastic bandage, it should cause slight obstruction to the return of the blood, but not sufficiently firm as to obliterate the pulse beat below or be in the least way annoyable to the patient.

The technique is correct if there is absolutely no increase of pain, and if there is visible hyperemia of the parts subjected to treatment; the portion distal to the bandage must appear bluish or bluish red—never white. All dressings should be removed while the compressing elastic bandage is in place, the wounds or bruises being covered with sterile gauze kept in place by a loosely applied towel. Under hyperemic treatment any abscess must be opened and pus evacuated.

Acute inflammatory processes require application of the hyperemic treatment for twenty to twenty-four hours per day. In chronic cases, especially if tuberculous, shorter sittings, from two to four hours per day.

In the use of suction apparatus or cupping glasses to produce obstructive hyperemia, the skin should turn red or bluish red, but never white; circulation must not be interrupted. The vacuum apparatus of large size is supplied with a suction pump. These suction glasses are applied for five minutes, six times daily, with intervals of three minutes between applications, in order to give the edema and hyperemic swelling an opportunity to disappear. Thus the entire time of treatment is three-quarters of an hour each day.

Treatment of acute abscess by **passive congestion** has given excellent results. Cases of purulent arthritis, suppuration of tendon sheaths, and acute abscesses and carbuncles have shown without exception almost immediate relief of pain and reduction of inflammation. The abscess either became "cold" or its contents changed to serum or were resorbed. Purulent arthritis was treated with passive motion after all pain had been relieved. The writer selected 15 of the 110 cases cited for brief description in the article. All cases were quickly cured, and it was only rarely necessary to open the abscess. Of the 15 cases reported, 8 were resolved, 3 were opened, and 4 were discharging when admitted. Bier (Münch. med. Woch., Jan. 31, 1905).

By means of **artificial hyperemia** we can often abort an infective process and save the breaking down of tissue, or, if at the beginning of treatment the process has gone on to the breaking down of tissues, the hyperemic method assists in quickening the process of expulsion of the products of infection and also the process of repair. J. H. Beaty (Jour. Minn. State Med. Assoc., Jan. 15, 1908).

In the use of hot air to produce hyperemia we produce an arterial hyperemia which differs from the obstruction or venous hyperemia. The effect of **hot-air hyperemia** is also different upon the body and also upon the pathologic process. This last method is apparently not used in the treatment of abscess.

The author comments on the value of **Wright's solution of sodium chloride, 4 per cent., and sodium citrate,** 1 per cent., as an agent for promoting drainage of abscesses. The hypertonic solution of sodium chloride by osmosis brings about a flow of lymph through the abscess walls, while the sodium citrate, by precipitating the calcium salts in the lymph, prevents the latter from clotting, and thus perpetuates the discharge. The lymph and 4 per cent. salt solution both antagonize the bacteria.

The technique of treating an abscess by this plan is described as follows: The abscess is opened by a wound as small as will allow the cavity to be wiped out, or thoroughly emptied by

expression. The surrounding skin is well cleaned with 70 per cent. alcohol and smeared up to the very mouth of the wound with boric acid or eucalyptus vaselin, in order to avoid skin irritation from the salt solution. If the skin tension closes the opening a bit of rubber dam may be put in. The wound is covered with a voluminous pad of gauze or of absorbent cotton covered with gauze, dripping wet with hot salt and citrate solution. A many-tailed bandage or some other application holds the poultice in position, and the part is put at rest. Outside the dressing may be applied a hot flaxseed poultice or a hot-water bottle. In any case, as often as the dressing gets cold, more of the hot solution is poured over the whole dressing to wet and warm it again, or the dressing is removed and the whole part soaked, if possible, or bathed with the same solution.

The solution is contraindicated if there is a tendency to persistent oozing of blood from the wound, and where the formation of protective adhesions is desirable.

Inguinal and axillary bubo, abscess of neck, septic fingers, mastoid wounds, otitis media after paracentesis, all drain well under this method. The solution should be used only for the first thirty-six to seventy-two hours after operation, during the acute stage of inflammation. The wound is then filled with glycerin or balsam of Peru. L. R. G. Crandon (Annals of Surg., Oct., 1910).

The **iodoform bone-wax** recommended by von Mosetig-Moorhof tried in 5 cases, in which the wax failed and was discharged. It is of value as a filling in selected cases of circumscribed abscess cavities in bone. Its use shortens the convalescence and makes the dressings easy and painless. Simmons (Annals of Surg., Jan., 1911).

Bismuth paste injection is an agreeable procedure for the physician and patient, practically painless and free from risk, and of value in the treatment of chronic fistulæ and abscess cavities. It is an excellent diagnostic auxiliary for determining the course and point of origin of fistulæ and abscesses, and, therefore, of great value in preventing incomplete and useless operations. The bismuth injections exert a pronounced effect in relief of symptoms by diminishing pain and secretion and curing eczema, and in some cases suffice to effect a complete cure. H. H. Schmid (Wiener klin. Woch., Nu. 7, 1911).

Antiferment Treatment.—This so-called "physiologic treatment" was recently introduced by Müller and Peiser. It is based on the antagonistic action the proteolytic ferment derived from leucocytes is supposed to meet from an antiferment in the blood-serum, especially in morbid effusions. This antiferment can be obtained from the patient's own blood-serum, after venesection or from puncture fluids. The contents of the abscess being aspirated, the antiferment is then injected into the cavity with the same needle, enough being introduced to fill it without distending it. The contents of the abscess are then again removed and the cavity is once more filled with fresh antiferment. This is repeated the next day if the area is still sensitive, the antiferment being left in. This method has not as yet been tried sufficiently to warrant an expression as to its merits.

No incision is required with this technique; it is applicable only when a mastitis or other process is tending to abscess formation. Thirteen typical cases of abscesses, felons, etc., are described out of an experience of 100 cases, to show the advantages of this treatment. The antiferment attracted to the spot is probably the main factor in the benefit from hyperemic treatment. A serum rich in **antiferment** can be kept on ice for several weeks in stoppered vessels. It should be tested from time to time to determine its strength. The larger the proportion of antiferment, the better and longer the

serum keeps. Müller and Peiser (Beiträge z. klin. Chir., Oct., 1908).

The **antiferment serum** not only supplies the ferment which protects against proteolysis, but at the same time it supplies vitally active leucocytes, opsonins, complements and amboceptors, either supplying them from without or attracting them to the spot, and thus summoning the most powerful defenses of the organism. Kolaczek (Beiträge z. klin. Chir., Dec., 1908).

The writer does not use the ready-made ferment, but injects a solution of **sodium nuclein** to induce leucocytosis in the tuberculous abscess. This is supplemented later by **Roentgen-ray** treatment. His first case was a tuberculous abscess in the soft parts of the thigh, which healed completely in three sittings after it had long resisted ordinary treatment. Goldenberg (Münch. med. Woch., Jan. 5, 1909).

Results in Dollinger's surgical service at Budapest with the Müller antiferment treatment in 160 cases. This physiological treatment proved satisfactory in nearly every instance. Its special field is for abscesses unless they are unusually extensive and deep, or the patient much debilitated, in which case incision is necessary; otherwise all that is necessary is to paint the outside with **iodine, aspirate** the contents of the abscess with a puncture needle and then inject pure **serum,** thus rinsing out the cavity, after which serum to an amount representing one-third or one-half the amount of abscess contents withdrawn is injected, and a scrap of gauze is laid over the puncture hole and held in place with a strip of plaster. An abscess containing from 1 to 5 c.c. of pus heals in three days; larger ones, containing from 20 to 50 c.c. of pus, heal in about eleven days. The absence of a scar is one of the great advantages of the method, and the functional result is always better, as conditions are more physiological. The writer has never encountered any signs of anaphylaxis, and the abscess never progressed except in a single instance, in a very debilitated patient. Gergö (Deut. Zeit. f. Chir., Jan., 1910).

The writer has tried the injection of **leucofermantin** into abscesses—a treatment based upon the fact that a proteolytic ferment is found in the polymorphonuclear leucocytes. A fairly large needle was used for aspiration and injection, and, after evacuating the abscess, he injected and withdrew a small quantity of serum, so as to clean out the cavity as thoroughly as possible before making the final injection, which was allowed to remain; a moist aseptic dressing was then applied. If the aspiration had to be repeated, the needle was inserted through the old puncture, so as to save pain. The quantity of serum left in varied, according to the size of the abscess, from 2 to 15 c.c. The author feels convinced that the principle on which the method is based is sound, and that it opens up a new pathway in the physiological treatment of suppurative inflammation. MacEwan (Brit. Med. Jour., Jan. 22, 1910).

Antiferment serum exerts a slight degree of curative action upon suppuration, but must be brought into intimate contact with the whole of the suppurating surface. It is suited only for superficial, well-defined abscesses. Boit (Med. Klinik, Apr. 16, 1911).

Surgical Measures.—Incision and drainage tersely indicate the surgical treatment of acute abscess. If suppuration cannot be avoided, the abscess should be opened under rigid asepsis, as soon as an adequate quantity of pus has formed to constitute an abscess sufficient in size to be recognized by the surgeon as such (Senn), or as soon as the presence of pus has been determined by the exploring needle or syringe. An early incision prevents excessive loss of tissue, less deformity and leaves smaller scar.

If a local anesthetic is necessary, one of the following may be used: Twenty drops of a 1 to 5 per cent. solution of cocaine introduced sub-

cutaneously near the abscess; ether sprayed over the seat of the abscess until local numbness is experienced; chloride of methyl or chloride of ethyl vapor. The latter is especially efficacious; the parts turn white when ready,—generally in about two minutes. Seltzer water spurted over the surface may be used to advantage when none of the other agents can be obtained.

To open an ordinary abscess a single small incision suffices; but, if it is large, several small incisions should be made to render perfect evacuation of its contents possible by drainage. If the abscess is superficial, the skin alone should be cut, but if it is deep seated the skin and fascia should be incised and the grooved director, or the points of a pair of forceps, used to reach the pus, the opening being kept patent with forceps. The cavity is then thoroughly emptied and syringed out with 1:10,000 **corrosive sublimate solution**, or, better, with **normal salt solution** or **boric acid solution**, until the fluid comes out perfectly clear. Pressure with the fingers is to be avoided, but loose necrotic tissue should be removed if it can be done without injury to surrounding structures. The incision and its surroundings are then carefully washed with one of the solutions mentioned, and an aseptic drainage-tube inserted. The wound is dusted with iodoform or dermatol, and an antiseptic dressing is applied, exerting slight pressure with bandage. If the abscess is deep, the drainage-tube should be shortened daily; if it is superficial, the drainage-tube can be withdrawn the second or third day.

Drainage by means of rubber drainage-tubes of sufficient size is preferred to the use of gauze. Two tubes placed side by side facilitate irrigation when necessary.

> A good plan is to **incise** the abscess freely, evacuate its contents, wipe off the wall with 10 per cent. **iodoform gauze**, aided by the curette, clean the cavity as perfectly as possible, using gauze freely to wipe out all *débris*. The wound is closed with sutures placed as deeply as possible to approximate wide areas of tissue. Pressure is kept up over the abscess to prevent its filling with serum, and a firm antiseptic dressing is applied. The result in the majority of cases has been excellent. In only 7 cases was there any breaking down of the wound and a resulting sinus. Iodoform emulsion was abandoned on account of the dehydrating action of the glycerin. In 48 of his cases the cavity has remained perfectly closed and aseptic for periods varying from four months to six years. Starr (Brit. Med. Jour., Oct. 13, 1906).

When it is necessary to traverse the peritoneal or pleural cavity in order to reach a collection of pus, infection may be avoided by carefully packing off the cavity with gauze, so as to form a sort of well with the abscess at the bottom.

The kind of dressing used after the abscess has been opened will depend upon the condition of the parts. If there be much infiltration of the tissues, swelling, and pain, a hot, moist antiseptic dressing is to be applied, as it favors absorption and is at the same time soothing to the patient. Any weak antiseptic solution (barring carbolic acid for fear of gangrene) may be used, as **boric acid, bichloride of mercury** (not stronger than 1 to 20,000), or **normal salt solution.** The dressings (wet or dry) while sufficiently firm to favor collapse and adhesion of abscess walls should yet

be loose enough to permit of easy absorption and evaporation of discharges. A generous dressing of gauze covered with absorbent cotton is advised.

Thirty-two cases of abscess treated by the Otis method: The skin about the affected area is scrubbed with green soap and washed with **sulphuric ether** and then with **bichloride** (1 to 1000). A narrow bistoury is then inserted into the abscess cavity, and the contents gently, but thoroughly, squeezed out; the cavity is irrigated with bichloride (1 to 1000) and immediately filled to moderate distention with warm **iodoform ointment** (10 per cent. iodoform and vaselin), care being taken not to use a sufficient degree of heat to liberate free iodine. An ordinary glass gonorrheal syringe is used, the plunger being removed, and the barrel warmed in the flame of an alcohol lamp and filled with ointment by means of a spatula. On finishing the injection, at the instant of withdrawing the syringe from the wound, a compress wet with cold bichloride solution is applied, which instantly solidifies the ointment at the orifice, preventing the escape of that into the abscess cavity. Edwin M. Hasbrouck (N. Y. Med. Jour., June 13, 1896).

Puncture and **disinfection** recommended for abscess instead of incision and drainage, in order to avoid mutilating scars and slow convalescence. The writer's method is as follows: 1. After careful disinfection, and under infiltration anesthesia, he punctures the most dependent portion with a large trocar or pointed scalpel, and gently expresses the pus. This is better than aspiration. 2. The cavity is then thoroughly irrigated through the trocar with a 1 : 1000 solution of **corrosive sublimate.** This can be used in large quantities, as the abscess wall does not absorb. He has found this strength most satisfactory. 3. The remnants of the corrosive sublimate solution are carefully squeezed out and the abscess is partly distended with a solution of from 5 to 10 per cent. **iodoform glycerin.** A moist dressing with a firm pressure bandage is then applied. This method is useful in every form of acute external abscess, following the principle originally laid down by Henle for cold abscess. To date the writer has treated 37 cases with good results in all except abscesses of caseous tuberculous glands, which generally required a secondary curetting, though they were none the worse for the preliminary conservative treatment. DeWitt Stetten (Jour. Amer. Med. Assoc., May 11, 1907).

Peroxide of hydrogen is prophylactic and curative medicament in the treatment of suppurative skin lesions so common in infants. A twelve-volume solution is ample as a skin-wash twice daily. This rapidly cures superficial lesions. Abscesses must obviously be evacuated before the peroxide solution is used. Cochart (Jour. de Méd. de Paris, April 21, 1901).

Personal method. 1. Cleanse the skin as in operating on sterile tissues. 2. Make an **incision** long enough to permit of the pus being freely evacuated and the pyogenic membrane rubbed clean and smooth with gauze wrapped around the finger. 3. Having emptied the abscess cavity as completely as possible, pack it tightly with gauze (1 to 1000 **mercury bichloride gauze,** dry) and apply a wool dressing and bandage as firmly as possible. 4. At the end of forty-eight hours remove the packing and dress the wound as if it were a simple incision, that is, do not pack or drain at all, but simply fix a gauze and wool dressing firmly in place with a bandage. This dressing will require changing only once in three or four days until the incision is soundly healed, the sides of the abscess cavity will unite promptly, and there is no outpouring of pus from it. From the time when the packing is removed it is practically a simple incised wound that is being treated.

There results rapid healing; the constitutional symptoms are gotten rid of almost at once; as the dressing requires renewal very seldom the doctor can do it himself and so avoid the risk

of a secondary mixed infection. J. Phillips (Brit. Med. Jour., May 16, 1908).

COLD, OR TUBERCULOUS, ABSCESS.—Symptoms.—These abscesses frequently attain a large size, and last for months without their presence being detected. Besides failing general health, the symptoms of the causative trouble are the only prominent ones. The spine, the hips, the genitourinary tract, and the lymphatic glands are the organs most prone to tuberculous disorders giving rise to cold abscesses. They sometimes appear several months and even years after the beginning of the primary disease.

The *general symptoms* of tuberculous abscesses do not closely resemble those of ordinary suppuration, but vary with the resisting powers of the individual. There is nearly always a slight evening rise in temperature (hectic) followed by a subnormal temperature in the morning. Loss of flesh and strength and the presence of anemia, more or less marked, are usual, although they may not occur unless mixed infection (tubercular and purulent) takes place. There is no leucocytosis. Amyloid (albuminoid) degeneration may appear as a later phenomenon.

The *local symptoms* are as a rule very slight, and are indicative of the effects of pressure upon organs or nerves rather than activity in the abscess itself. Large fluctuating abscesses may exist in various parts of the body, even about joints, without serious discomfort to the patient. No pain is experienced as a rule; cold abscesses are not even tender to the touch. There is no redness until the abscess is about to break, the focus of the liquid mass being otherwise too deeply seated, the skin covering the abscess remaining white or normal in color unless the abscess be just beneath the surface, which phenomenon has caused the name "white swelling" to be applied in tuberculosis of the knee.

The above symptoms usually follow or are coincident with the sudden appearance of a swelling. Though generally soft, it may be hard, and suggest a tumor in the vicinity of the spinal column (Pott's disease), above or below Poupart's ligament, after burrowing along the psoas muscle (psoas abscess), on the inner aspect of the thigh, or in the lumbar region (lumbar abscess), etc. In the neck cold abscesses are usually due to disease of the neighboring cervical lymphatic glands. The skin either remains normal or gradually becomes thinned and softened until an external opening is formed.

Fluctuation, usually detected with ease, is sometimes hidden by a thick investing layer of lymph, which gives the mass a peculiar tension, suggesting a lipoma or some other hard growth. Aneurisms sometimes convey the sensation produced by a cold abscess: a fact to be borne in mind when operative procedures are under consideration.

Pathology.—A cold abscess can always be traced to a specific inflammatory process, and almost invariably to one of a tubercular nature. Where the confluent masses in the center of a nodule begin to break down, there is formed a collection of material surrounded by tuberculous tissue. This material becomes infiltrated with leucocytes, and thus is produced a cavity containing fluid fatty material, frag-

ments of cells, and leucocytes, around which there is granulation tissue filled with tubercles. In this way a tuberculous abscess is formed. It seems at times to be quite a matter of accident whether the abscess breaks into the joint or finds its way by a more circuitous route into the surrounding connective tissue. As the tuberculous masses spread, caseation takes place at different points in the wall, and the masses are discharged into the cavity of the abscess; but the spread of the abscess is effected generally by what is termed "burrowing of pus." This burrowing occurs in various directions, and large collections of pus altogether out of proportion to the original lesion are formed, and are known as cold abscesses.

What has been called a chronic abscess is very often no abscess at all. In tubercular processes the product of tissue proliferation undergoes coagulation necrosis, and disintegrates into a granular mass, which, when mixed with a sufficient quantity of serum, forms an emulsion that microscopically resembles pus, but under the microscope shows none of the histological elements which are found in true pus. An abscess can only be called such if it contains pus. A true chronic abscess can originate in a tubercular, actinomycotic, or syphilitic lesion, when the granulation tissue is secondarily infected by the localization of pus-microbes, which convert the embryonal cells into pus-corpuscles.

Differential Diagnosis.—The concomitant disorder usually makes a diagnosis easy in a case of cold abscess; but occasionally the swelling is the only indication of ill health, and it is important to determine, under such circumstances, the nature of the pus. The macroscopical appearances of "laudable" pus and of "sanious" pus are frequently so similar that a *de visu* diagnosis is not justified. Bacteriological examination of the contents of such abscesses will show conclusively whether they are true pus-containing abscesses or whether or not they are pseudo-abscesses. If cultivations are made of their contents, pus-microbes will grow upon proper nutrient media if it be a true abscess, while from the contents of a pseudo-abscess only the microbes of the primary infection can be cultivated. The information obtained by the discovery of the essential cause can be confirmed by inoculation experiments.

Prognosis.—The walls of cold abscesses are usually tense and tough, and are lined with cheesy tuberculous material. They do not tend to collapse, as is the case with acute abscesses, and for that reason are healed with difficulty. When, however, the seat of the original trouble can be reached and successfully treated, the fluid in the parts of the abscess tract is absorbed, and the caseous matter undergoes calcification. This fortunate issue of the case is seldom met with, however, and the abscess usually continues, the primary etiological factor acting as a drain for the diseased area. The prognosis, therefore, depends upon the result obtained in the treatment of the latter.

Surgical Treatment. — Experience has shown that when such a cold, or tuberculous, abscess opens spontaneously, or is incised in a careless way, profuse suppuration and hectic fever follow, with only too often a speedy fatal result from septic infection.

Unless the surroundings of the patient admit of carrying out the antiseptic treatment to its full and perfect extent, a chronic abscess should not be evacuated by incision. It should be aspirated. When an incision can be made, it should be free, and the cavity should be thoroughly curetted, cleansed, irrigated with normal salt solution or a solution of boric acid, disinfected, and iodoformized, then sutured, drained, and treated as a recent wound.

The early recognition of cold abscesses will enable one to dissipate or to nip them in the bud. When they are present at the time the cases come under observation, they should be treated with indifference so long as they do not interfere with the proper adjustment of good protection apparatus. If they are in the way, or if they show a disposition to burrow and encroach on parts that it is desirable to keep free from such invasion, **aspiration** should be resorted to and cultures made in order to determine their virulency. If aspiration fails, **incisions** under rigid asepsis, large enough only to permit evacuation of the contents, should be relied on, and the introduction of chemicals should be refrained from. The wound should be closed by suture under the same rigid asepsis. When the abscess lies directly over a bone focus that can be easily reached, the incision should be made large enough to remove the focus, and at the same time permit removal by curette or scissors of the lining of the sac and all necrotic tissue contiguous thereto. It should then be closed aseptically, employing drainage for not over forty-eight hours. If longer drainage is demanded, means should be devised by which asepsis in dressings may be continued indefinitely, and a mixed infection looked on as a calamity. Sinuses should be well drained, the foci on which they depend should be treated if involving joints by perfect and long-continued immobilization, with due regard to fresh air and a high state of nutrition. V. P. Gibney (Jour. Amer. Med. Assoc., Oct. 29, 1904).

Conclusions based on 26 reported examinations of tuberculous abscesses: Tuberculous abscesses will frequently disappear under thorough protective treatment, and will not require an incision. Exploratory puncture of the joints should be made early, and of the abscess preceding any operation, for diagnostic purposes. The method of operation should be decided on from the results of the laboratory examinations. When the abscess is reported sterile it should be thoroughly incised, curetted, and closed without drainage, under the most careful aseptic precautions. When the abscess report shows large numbers of tubercle bacilli, the incision should be cauterized before the sac is incised, with thorough curettage, partial closure, and drainage for not over forty-eight hours, the strictest asepsis being maintained.

When the cultures show mixed infection the abscess should be incised, thoroughly curetted, washed with a formalin solution, partially closed aseptically, and drained for not over forty-eight hours. If the clinical symptoms and X-ray show an accessible focus of disease this should be thoroughly removed at the same time the abscess is incised, by curettage, erasion, partial closure, and drainage for a short period. Cultures should be taken from sinuses, and, if sterile, the sinus should be treated by absolute, thorough, and complete immobilization of the tuberculous area, with partial closure and aseptic dressings. If the cultures taken from the sinuses show tubercle bacilli the part should be thoroughly curetted, immobilized, and treated with a saturated solution of methylene blue. If the cultures from the sinuses show mixed infection they should be thoroughly curetted under strict aseptic precautions, the diseased part should be immobilized, and the general condition should be treated by **serum therapy.** Young (Amer. Jour. of Orthop. Surg., July, 1907).

On general principles, necrosed or detached bone should be looked for in all cases. Strict antiseptic precautions are imperative to avoid mixed infection (bacilli of tuberculosis and pyogenic cocci). Preliminary precautions should be taken to meet violent hemorrhage due to vascular erosion.

When there is local inflammation and spontaneous opening of the abscess is probable, there should be a free incision, a thorough scraping of its walls with Volkmann's curette to transform the suppurating surfaces into bleeding ones. The cavity is then cleansed with a 5 per cent. solution of **carbolic acid,** a long drain is applied, and the wound is stitched as far as the drain. An antiseptic dressing is then applied. (Volkmann, Trélat, Pozzi.)

After opening the abscess the cavity may be washed out with **peroxide of hydrogen** in 10 per cent. solution or packed with **iodoform gauze.** Removal of the limiting sac is then performed by **decortication,** the steps being: free incision, the sac detached with finger or spatula and removal, and the cavity closed immediately. (Lannelongue.)

The removal of the limiting sac is facilitated by filling the wound with **paraffin**; the mass can then be removed as if it were a lipoma. (Cazin.)

A psoas abscess should be opened in the loin and groin when possible. In the loin the incision should be made through the external and internal oblique, transversalis, and lumbar fascia, along the outer edge of the erector spine to the edge of the quadratus lumborum. The latter muscle and the transversalis fascia are divided on a level with the tip of the second or third lumbar transverse process, avoiding the lumbar arteries. The sheath and the psoas are then perforated with the finger or a trocar. A counteropening is then made below Poupart's ligament to form a tunnel, into which a large-size drainage-tube is inserted. This is replaced, later on, by a tube at each end to obtain obliteration, beginning from the center of the canal. If one incision is preferred the loin should be selected.

Aspiration and Injections. — When no local inflammation indicates that the abscess is soon to open, the fluid may be withdrawn with a large aspirator; a 5 per cent. solution of **carbolic acid** is injected and then aspirated. This procedure is renewed until the solution withdrawn is perfectly clear. A Lister bandage is then applied, insuring slight pressure. Five days later the treatment is renewed. About five sittings are required. (Boeckel.)

Injection fluids: **Iodoform,** 1 part; **ether,** 5 parts; **distilled water,** 5 parts. Injection not to be renewed while iodoform is being excreted in the urine. (Mosetig-Moorhof, Verneuil.)

Less painful is a mixture of 1 part of **iodoform** to 10 of **glycerin** (Billroth) or of **olive oil** (Bruns).

Intoxication may be prevented by sterilizing the iodoform and excipient (except ether) by heating at 212° F. separately. (Tillmann.)

> Mixture used for injections into cavities of tuberculous abscesses after aspiration: **Iodoform,** 5 grams; **ether,** 10 grams; **guaiacol** and **creosote,** 2 grams of each, and **sterilized olive oil,** 100 c.c. Solutions of iodoform combined with ether were also commonly used. Out of 29 cases of spinal caries with abscesses, 27 were cured, 2 remain with sinuses which are not infected and in which the discharge is diminishing and the general condition is good. There were 33 cases of hip disease; of these, 32 patients were cured, 1 remained with a sinus. In this case the sinus was serious, due to a secondary

infection caused by improper sterilization. The number of aspirations was from 1 to 21 in each case. At a cripples' home 23 closed tuberculous abscesses connected with lesions in the spine, hip, and knee were treated by aspiration; 8 spinal abscesses were aspirated. The greatest number of aspirations required for any one case was 12; the average number required was 3. All the patients are apparently cured, and in no case has a sinus formed. Thirteen cases of abscess in connection with tuberculous disease of the hip were treated by aspiration. Of these 12 patients had been apparently cured. In 1 case a small sinus persists, but is not infected. The greatest number of aspirations required for any one case was 14. The average number was 4. Two abscesses in connection with the knee-joint have been similarly treated, and both patients are apparently well. Calve and Gauvain (Lancet, Mar. 5, 1910).

Boric acid, a 4 per cent. solution, may be used as above (Ménard), or **naphthol** and **camphor,** 1 part each. About thirty sittings are usually required.

The lesion being a tuberculous one, the general system should be treated accordingly. **Nutritious food,** including a free supply of milk and eggs, **pure air, sunlight,** and **sea-air,** if possible, are indicated, as well as **tonics** and **alteratives** (**codliver oil** and **hypophosphites, iodine, iodides, arsenic, quinine, strychnine,** etc.).

In the Middlesex Hospital, London, Kellock obtained good results from the use of **sulphur** in tuberculous sinuses and cavities, and remarks the superiority of this agent over iodoform under similar conditions. J. R. Eastman (Jour. Indiana State Med. Assoc., Jan. 15, 1908).

One hundred cases of tuberculous abscess, including tuberculosis of bony structures, joints, lymph-glands, tendons, etc., were treated with **trypsin** by the writer. The procedure is described as follows: 0.1 Gm. of trypsin is introduced in sterile flasks of 10 c.c. size, and the mouths of the flasks plugged with cotton. Before using, each flask is filled with normal saline, giving a 1 per cent. solution of trypsin. The mixture should be freshly prepared each day, as it is unstable. The abscesses are entered with a large trocar and emptied as much as possible by pressure. One to 2 cm. of the trypsin solution is then injected and the opening covered with adhesive plaster. Injections are given every five to seven days. Joint cases are always immobilized in plaster dressings.

After a few injections the pus, originally yellowish, assumes a brownish-red color, owing to admixture of blood, and resembles an emulsion. This method gives good results in "ganglion" and cold abscesses of small size. Small, bony foci may also be cured. In burrowing abscess formations trypsin has no particular advantage over iodoform and glycerin. It should not be used at all in cases of joint tuberculosis with extensive bony foci, or in lymphatic foci which have not yet become softened or are in the stage of caseation. No untoward results followed the injections, except slight pain, lasting a half to one hour, and in some instances a painful edema surrounding the focus, generally only temporary, but sometimes persistent. A. Brüning (Deut. med. Woch., Sept. 1, 1910).

C. Sumner Witherstine,
Philadelphia.

A. C. E. MIXTURE. See Chloroform.

ACETANILIDE. — *Acetanilidum,* formerly known under the name of *antifebrine,* is obtained by boiling aniline with glacial acetic acid. It is the monacetyl derivative [C_6H_5.NH.-CH_3CO] of aniline.

PROPERTIES. — Acetanilide occurs as a white or colorless shining powder or as crystalline laminæ. It

is odorless, but has a slightly burning and bitter taste.

DOSE.—The dose of acetanilide is 3 to 5 grains (0.2 to 0.325 Gm.) in adults; the tendency, however, is to employ smaller quantities. In children, according to Griffith, the coal-tar products of this class are well borne; ¼ to ½ grain (0.016 to 0.033 Gm.) may be given at 6 months, increasing the dose by ¼ grain with each year, until the adult dose is reached. The action of acetanilide should be closely watched in weak subjects and in hysterical women.

> Out of 274 observers who stated that they used acetanilide, 17, or 6.2 per cent., employed less than 2 grains as a minimum dose for adults; 113, or 41.2 per cent., employed 2.5 grains or less as a minimum dose, and 155, or 56.5 per cent., employed from 3 to 5 grains as a minimum dose. Two hundred and forty, or a little over 87.5 per cent., never exceeded a dose of 5 grains, and 34, or not quite 12.5 per cent., employed doses exceeding 5 grains.
>
> An examination of a number of prescriptions for adults on file in various pharmacies in Washington, D. C., brought into court as evidence, showed the average dose of acetanilide prescribed was 2.43 grains. Kebler, Morgan and Rupp (U. S. Dept. of Agricul., Bureau of Chemistry, Bulletin No. 126, July 3, 1909).

MODES OF ADMINISTRATION.—Acetanilide is insoluble in glycerin, slightly soluble in water (1 grain in 3 fluidrams of cold, and 1 grain in 18 minims of hot, water), but completely so in alcohol (1 grain in 2½ minims), and readily in ether (1 grain in 18 minims). It is readily suspended in syrupy mixtures and can be given with most drugs thus administered. Acetanilide is also dispensed by druggists in the form of tablets, which are quite tasteless when taken with a mouthful of water. It may be given in the form of powders or in dilute alcoholic solutions.

There is also available the official compound acetanilide powder (*pulvis acetanilidi compositus*), containing acetanilide, 7 parts; caffeine, 1 part, and sodium bicarbonate (to increase the solubility of the acetanilide), 2 parts, the dose of which is 5 to 10 grains (0.3 to 0.6 Gm.).

> While acetanilide is not soluble and is readily suspended in syrupy mixtures, it can be combined with ammonia in any of its forms, salicylic acid, nux vomica, digitalis, codeine, creosote, potassium bromide, etc. A prescription can therefore be elaborated that can be much more accurately adapted to the case in hand than any of the ready-made combinations. The foundation of most of the coal-tar product combinations is acetanilide, which has been combined with bicarbonate of soda, caffeine, carbonate of ammonia, etc. The combination may be chemical or mechanical, it matters little which, as it is practically broken up in the body into acetanilide radicals and other constituents. L. Faugères Bishop (Med. News, June 10, 1899).
>
> Various combinations of acetanilide with other drugs (adjuvants and corrigents) may be made to meet the exigencies of practice, some of which are as follows:—
>
> ℞ *Acetanilidi* ..... gr. xij (0.800).
> *Caffeinæ citratæ* .... gr. iij (0.200).
> *Camphoræ monobrom.* ..... gr. vj (0.400).
> Misce et fiant capsulæ no. vj.
>
> NOTE.—The caffeine and camphor are used as corrigents to the acetanilide.
>
> ℞ *Acetanilidi* ..... gr. xv (1.000).
> *Sodii bicarbonatis* .. gr. x (0.650).
> *Ammonii carbonatis*. gr. xv (1.000).
> Misce et fiant capsulæ (not pulveres) no. x.
>
> NOTE.—The sodium bicarbonate aids in the assimilation of the acetanilide, while the ammonium carbonate acts as a corrigent.

℞ *Acetanilidi* ..... gr. xx (1.300).
Sodii bicarbonatis. gr. xv (1.000).
Caffeinæ ..... gr. vj (0.400).
Acidi citrici ..... gr. x (0.650).
Misce et fiant capsulæ (not pulveres) no. x.

NOTE.—The caffeine and citric acid in the above should be mixed and slightly moistened; this allows the formation of a fresh preparation of citrated caffeine; it should then be dried and mixed with the other ingredients.

℞ *Acetanilidi* ..... gr. xx (1.300).
Sodii bicarbonatis. gr. xx (1.300).
Sodii salicylatis . ʒiss (6.000).
Misce et fiant chartulæ no. x.

NOTE.—The sodium salicylate is used as a synergist to the acetanilide.

℞ *Acetanilidi* ..... gr. xx (1.300).
Potassii bromidi . gr. xxx (2.000).
Sacchari lactis .... gr. xv (1.000).
Misce et fiant chartulæ no. vj.

NOTE.—The potassium bromide is used as a synergist to the acetanilide.

℞ *Acetanilidi* ..... gr. xxv (1.600).
Potassii bromidi . gr. xv (1.000).
Caffeinæ citratæ . gr. v (0.325).
Misce et fiant capsulæ no. x.

℞ *Acetanilidi* ..... gr. xxv (1.600).
Sodii bicarbonatis. gr. x (0.650).
Caffeinæ citratæ . gr. vj (0.400).
Camphoræ monobromatæ ..... gr. vj (0.400).
Misce et fiant capsulæ no. x.

℞ *Acetanilidi* ..... gr. x (0.650).
Sodii bromidi .... gr. L (3.250).
Extracti hyoscyami ..... gr. v (0.325).
Caffeinæ citratæ . gr. v (0.325).
Morphinæ sulphatis. gr. ⅕ (0.013).
Misce et fiant tabellæ (or capsulæ) no. x.

NOTE.—The sodium bromide, extract of hyoscyamus, and morphine sulphate all act as synergists to the acetanilide, while the caffeine corrects their action.

℞ *Acetanilidi* ..... gr. xx (1.300).
Quininæ sulphatis gr. xx (1.300).
Extracti hyoscyami ..... gr. v (0.325).
Extracti cannabis Ind. ..... gr. iiss (0.163).
Arseni trioxidi .. gr. ⅒ (0.0065).
Strychninæ sulphatis ..... gr. ⅕ (0.013).
Misce et fiant tabellæ (or capsulæ) no. x.

NOTE.—The strychnine sulphate is used instead of the caffeine as a corrigent.

℞ *Acetanilidi* ..... ʒj (4.000).
Zinci oxidi ..... ʒj (4.000).
Amyli .....q. s. ad ʒj (32.000).
Misce et fiat pulvis.
Sig.: Use as a dusting powder.

℞ *Acetanilidi* ..... ʒj (4.000).
Adipis lanæ ..... ʒij (8.000).
Petrolati ..q. s. ad ʒj (32.000).
Misce et fiat unguentum.

℞ *Antipyrinæ* ..... ʒj (4.000).
Caffeinæ citratæ .. gr. xx (1.300).
Aquæ destillatæ . fʒiv (120.000).
Misce et fiat solutio.
Sig.: Teaspoonful as required.

NOTE.—In the above prescription antipyrin is used, as it is very soluble, while acetanilide is almost insoluble. W. H. Foreman and J. H. Gertler (Jour. Indiana State Med. Assoc., June 15, 1909).

It has been supposed that the addition of caffeine to acetanilide decreased its toxicity, and, therefore, the likelihood of untoward effects. Hale has shown experimentally, however, that such was not the case, and, indeed, that it greatly increased it. Sodium bicarbonate, on the other hand, tends to lessen the toxic effects of acetanilide upon the heart.

By experiments on the hearts of warm- and cold- blooded animals the writer found caffeine of little or no benefit in acetanilide poisoning in so far as the cardiac energy and the blood-pressure were concerned, and that it apparently exerts a harmful effect in some cases. But there appeared, especially in the dog, to be a well-established antagonism on the heart rate which, however, would probably be insufficient to be of any value in cases of poisoning in man. Feeding experiments demonstrated the absence of antagonism between acetanilide and caffeine, in all cases the addition of the latter drug causing death more quickly or with a smaller dose. This, in connection with the imperfect antagonism to the heart action, makes the use of caffeine in acetanilide mixtures especially questionable. Sodium bicarbonate, in contrast, lessens the toxicity of acetanilide, both

in its action on the heart and on the intact animal, increasing the duration of life or making the use of a larger dose of acetanilide necessary to cause death. Hale (Jour. of Pharmacol. and Exper. Therap., Aug., 1909).

INCOMPATIBLES.— Acetanilide forms insoluble compounds with the bromides and iodides in aqueous solution, and a soft mass on trituration with chloral, carbolic acid, thymol, or resorcinol. According to Blackwood, unexpected and often alarming effects are observed when calomel is given with any coal-tar product.

CONTRAINDICATIONS. — Acetanilide should not be used when the heart is fatty, weak, or enlarged; in blood disorders such as pernicious anæmia characterized by cell destruction; in phthisis or other exhausting diseases, and in pregnant or nursing women.

It has been urged against the coal-tar derivatives that, although they relieve pain, they do not procure sleep. In the first place this is an error; they do induce somnolence, though this is much less marked than when opiates are used. But even were it true,—nothing prevents the simultaneous use of safe soporifics, such as the bromides or chloral hydrate. There is, in fact, a distinct advantage in their employment concomitantly, since the dose of either agent—acetanilide and ammonium bromide, let us say—can be made smaller, 2 grains of the former and 10 of the latter being quite sufficient in most cases to relieve pain and insure prolonged sleep. Antipyrin and phenacetin are quite as efficient when thus administered, but somewhat larger doses, 4 grains, are needed. Though acetanilide is not soluble in water, it is readily suspended in syrupy mixtures, which will also take up ammonium bromide very readily.

Far from being harmful, in the hands of the profession, the coal-tar derivatives have furnished us the only means to avoid the use of the opiates which, notwithstanding the great service they have rendered humanity, have left in their train victims in numbers untold, and the shadows of which hover at once before the modern practitioner's mind when he is called upon to alleviate suffering. Sajous (Monthly Cyclo. and Med. Bull., March, 1910).

PHYSIOLOGICAL ACTION.— **As Antipyretic.**—In the normal subject, the temperature, according to Nothnagel and Rossbach and most authorities, is lowered only when toxic doses are given. Not so, however, when fever is present. Here a small dose suffices to produce a marked fall. Dujardin-Beaumetz, for example, witnessed a decline of 3° C. (5.4° F.) and cyanosis in a case of typhoid fever in which 7½ grains (0.5 Gm.) had been administered. Manquat states that 1½ to 3 grains (0.1 to 0.2 Gm.) suffice to influence the temperature, acetanilide, according to Krieger, Cahn and Hepp, being far more active in this particular than antipyrine. Sweating and chills are occasionally observed.

The investigations of Hare and Evans suggested that the fall of temperature produced in febrile cases was due to a decreased heat-production and increased heat-dissipation. But Wood, having found that the *rectal* temperature not only did not fall as did that of the surface, but that it rose, concludes that the experiments of Hare and Evans "cannot be used to explain how antifebrin reduces the temperature." Moreover, most European investigators, Lépine, Podanowsky and others, hold that acetanilide acts by depressing the heat-center. According to Cushny, it affects the nervous heat-regulating mechanism in such a manner as to lower the level

at which the body-temperature is maintained, the loss of heat necessary to produce the fall in temperature being accomplished by dilatation of the cutaneous vessels. The manner in which acetanilide acts as an antipyretic is stated by Butler to be far from understood.

[The antipyretic action of acetanilide becomes plain when new factors, brought out by my own labors, are also taken into account. The adrenal and thyroid secretions (see "Internal Secretions," p. 1008) are the blood constituents which sustain general oxidation and metabolism. As the blood enters all tissues through their arterioles, constriction of these minute vessels must necessarily reduce the quantity of blood admitted into the tissues, and thus inhibit oxidation, *i.e.*, heat production. This is precisely what acetanilide brings about by exciting directly the sympathetic center, which, as I have shown (*loc. cit.*, p. 982), governs the caliber of the arterioles.

This mechanism explains, moreover, all the above experimental and clinical data. A small dose suffices to reduce fever, though inactive in the normal subject, for example, because the sympathetic center is already, during fever, the seat of undue metabolism and, therefore, oversensitive; cyanosis is produced by large doses because they constrict abnormally the arterioles and cause local accumulation of CO_2; chills are excited by lowering of the surface temperature caused by the deficient supply of arterial blood incident upon the constriction of the arterioles, etc. C. E. DE M. S.]

Action as Analgesic.—According to the prevailing view, acetanilide acts directly as a sedative upon the nervous system, especially upon the sensory portion of the spinal cord; with toxic doses the effect may extend to total loss of reflex action and sensory and motor paralysis, the muscles being influenced only directly. Wood holds that, "directly or indirectly, acetanilide affects the cerebral function," though at a certain stage of its toxic action consciousness may be uninfluenced while the rest of the nervous system is clearly affected. Bokaï ascribes the effects of acetanilide to paralysis of the motor nerve-endings in the muscles, sufficiently prolonged exposure of the latter to the poison also annulling their ability to contract. Cushny, referring to this and other coal-tar products, states that "by many they are supposed to have a sedative or depressant effect on the nervous system." The analgesic action of acetanilide is generally ascribed to this supposed sedative effect, though all agree that applied locally to the tissues it acts as a stimulant or mild irritant.

[These various opinions involve the assumption that a dose of acetanilide dissolved in the thirteen pints of blood the vessels of an adult contain will make a sufficiently strong solution to act directly on the central or peripheral sensory elements. Clinically such a solution in water, when injected directly into the tissues, has no local effect other than that produced by water without acetanilide. The above explanations have, therefore, no foundation in fact.

On the other hand, the analgesic action of acetanilide is clearly explained by the mode of action I have pointed out: By exciting the sympathetic center, it causes constriction of all arterioles, and, by thus reducing the volume of blood admitted into the diseased area, it counteracts the cause of the pain therein—the hyperemia. C. E. DE M. S.]

Action on the Blood.—The cyanosis produced by excessive doses of acetanilide is ascribed by Lépine, Hénocque and others to transformation of the hemoglobin into methemoglobin, and by Vierordt, Halliday and others to the reduced hæmoglobin as it occurs in venous blood. Some contend that the red corpuscles are disorganized, while others hold that they remain intact.

[When the dose is excessive or from one cause or another the sympathetic center is oversensitive, the arterioles are so constricted that the volume of blood admitted into the tissues is inadequate. The oxygen supply being deficient in proportion, the blood becomes venous prematurely and cyanosis ensues. When still further reduced the hemoglobin breaks down and methemoglobin appears in the blood.

The view of Vierordt and others that the cyanosis is due to reduced hemoglobin is thus sustained. But this applies as well to methemoglobinemia, since, as I have shown (see "Internal Secretions," 3d ed., pp. 102 and 828), this phenomenon is produced when the connecting link between the hematin and the albuminous constituent, the oxygen-laden adrenal secretion, is taken up by a powerful reducing agent—the tissues in the present instance. C. E. DE M. S.]

Action on the Circulation.—Injections of acetanilide in animals have been found to cause at first a slight increase in the number and force of the heart-beats, with corresponding rise of blood-pressure. Later, and also from the first with larger doses, circulatory depression is observed. In febrile patients the lowering of temperature produced by the drug is often accompanied by reduction in the frequency and size of the pulse. Large doses are said to depress the heart directly.

[These phenomena are the normal results of the exciting action of the drug upon the sympathetic center and the resulting constriction of the arterioles. Those of the heart admitting less blood into its muscular walls, the force of its contractions and their number are reduced. The heart's action may be arrested by the same process. C. E. DE M. S.]

UNTOWARD EFFECTS AND ACUTE POISONING.—The symptoms of poisoning include primarily the cyanosis, which begins at the lips and then extends, gradually becoming more intense, over the face and the rest of the body, and is accompanied by profuse sweating and prostration. In some cases there is ashen lividity and the temperature falls rapidly to 95° F. or lower. The pupils are dilated and fixed. The respiration is slow and shallow, and the pulse becomes steadily weaker and then irregular and fluttering. Somnolence, unconsciousness and coma, and cardiac arrest follow. In some instances sudden heart-failure occurs soon after the onset of the symptoms, the organ being arrested in diastole. Erythematous or urticarial skin eruptions and disorders of hearing are occasionally observed.

[Acetanilide proves toxic, from my viewpoint, when it causes sufficient constriction of the arterioles (by exciting the sympathetic center) to prevent the entrance of blood into the tissue capillaries, thus arresting function. As the vascular constriction increases, cyanosis deepens, and the skin becomes livid; the spiral muscles of the sweat-glands being deprived of blood, they are relaxed, and profuse sweating occurs; the pupillary sphincters being relaxed through the same process, the pupils dilate. The failure of the skeletal muscles to receive blood accounts for the prostration, while a similar deficiency of blood in the myocardium explains the weakening pulse and the cardiac arrest in diastole. The cerebral ischemia being no less complete, somnolence, unconsciousness and coma occur in more or less rapid succession.

The occasional presence of deafness is due to the inadequate supply of blood to the aural apparatus that results from undue constriction of the arterioles. The same process explains the cutaneous eruptions, since the slowing of the blood-stream in the tissues interferes with the carrying off of waste products from the skin. C. E. DE M. S.]

Case of a man, aged 45, suffering from a form of intermittent fever. The patient complained of almost unbearable headache; pulse, 120; respirations, 23; temperature, 104.8° F. Ten grains of acetanilide were given, and about twenty

minutes later the patient said his headache was relieved, and that he felt easier. About forty-five minutes after the drug was administered all sweating ceased, and a peculiar sensation of warmth under the skin was complained of. To this, in twelve or fifteen minutes, was added intense itching, while in three or four minutes the whole body presented a general erythematous condition. The entire surface was of a brighter red than that of a typical case of scarlet fever, and, like the scarlatina rash, it disappeared on pressure, to return as soon as pressure was removed. No part of the body was exempt from this rash, the conjunctivæ, palms of the hands and soles of the feet being as red as any part of the body. The temperature of the surface seemed elevated, but the thermometer in the mouth showed that it was gradually falling. The body appeared as if every superficial capillary was dilated.

With the appearance of the rash the itching became more intense, the patient assuming all positions possible while scratching. Within the external ear the itching was especially intense, but there was no disturbance of hearing. The rash lasted for six hours, without any apparent change, and then disappeared rapidly from all parts of the body simultaneously, and as the rash faded the itching subsided. About this time a slight cardiac irregularity became evident, and this lasted for four days. The only drug taken before the acetanilide was a single dose of calomel (about 5 grains). P. V. Ballou (Med. News, Jan. 18, 1898).

[The two unusual symptoms, intense itching and general erythema, were due to excessive dilatation of the arterioles after the true toxic effects had passed off, the violent excitation to which the poison had subjected the sympathetic center having temporarily exhausted it. C. E. DE M. S.]

Out of 288 practitioners questioned, 219, or 76 per cent., stated that they had observed instances of poisoning following the use of acetanilide. These 219 observers report 614 cases of poisoning, including 17 deaths, *i.e.*, 2.7 per cent.

The character of these cases and the doses used were as follows:—

Pneumonia (child)	One-half grain every 2 hours until 2 grains were taken.
Capillary bronchitis (child)	Small doses frequently repeated.
Capillary bronchitis (child)	Small doses frequently repeated.
Typhoid	Five grains every 4 hours
Headache	About 20 grains.
Headache	Thirty grains (?).
Headache	"Orangeine" taken freely
Headache	Thirteen or fourteen 5-grain doses in 12 hours.
Headache	Bromoseltzer.
Neuralgia	Dose not given.
Neuralgia of heart	Five 5-grain doses in 5 hours.
Burn	Boroacetanilide applied freely.
Burn (infant)	Acetanilide applied freely to umbilical cord.
Headache	Excessive doses of "bromoseltzer."
Typhoid (child)	Five grains.
Typhoid (child)	Dose not given.
Malaria (child)	One and one-half grains.

Kebler, Morgan and Rupp (U. S. Dept of Agricul., Bureau of Chemistry, Bulletin No. 126, July 3, 1909).

The great majority of such cases are due to intoxication by proprietary headache powders sold under a variety of fancy names. Proprietary preparations containing acetanilide were reported to have been used in 77, or 12.5 per cent., of the 614 cases of poisoning mentioned above by Kebler, Morgan, and Rupp. It is well known that certain individuals show an idiosyncrasy to the drug, and in some instances very small doses will suffice to cause death.

Case of acetanilide poisoning in a woman, aged 26 years, who had taken 8 grains. Collapse with strong convulsive movements, partial loss of consciousness, and great retching. **Whisky, strychnine nitrate,** and—for two hours—**artificial respiration** induced recovery. O. R. Summers (N. Y. Med. Jour., March 24, 1900).

Case of fatal acetanilide poisoning. The patient, a man of 37, had taken six "headache powders" each containing 10 grains. He became delirious, com-

plained of abdominal pain, vomited, and was slightly jaundiced. His temperature rose to 100.2° F., the lips and nails became intensely cyanotic, respirations shallow and frequent. The urine, of which 10 ounces were passed on admission, was nearly black and strongly alkaline. Anuria occurred, and six days later the man died. There was alternate constipation and diarrhea, and forty-eight hours before death the feces constantly showed blood-pigment, blood-clots, and corpuscles. Philip Brown (Amer. Jour. Med. Sci., Dec., 1901).

Case of acetanilide poisoning with fatal results following the ingestion of bromoseltzer taken to relieve a headache. The heart, already weakened from repeated doses of the drug, was unable to stand a slight overdose and the victim died in a few hours. H. B. Hemenway (Jour. Amer. Med. Assoc., Dec. 29, 1906).

Personal case in which the patient had taken four headache powders. These had been taken each hour between nine and noon. The surface of the body presented an ashen-gray appearance, the mucous membranes having a much darker hue. The temperature was 96 degrees; pulse, 60, and respiration, 10. **Digitalis, strychnine,** and **alcohol baths** with **friction** were employed, with **dry heat** to the surface. When the patient was able to swallow, a combination of **aromatic spirit of ammonia, brandy,** and **capsicum** was given. Twenty-four hours later the temperature was slightly subnormal, the dusky appearance of the face disappeared to a large extent, but the symptoms of cyanosis did not wholly vanish until the second day. The powders contained 3 grains of acetanilide, 2 grains of bicarbonate of sodium, and 1 grain of caffeine; hence the total dose was 12 grains of acetanilide. Earps (Merck's Archives, June, 1901).

The doses capable of producing toxic effects are sometimes very small, but it is probable that some of the drugs recommended in textbooks for the treatment of poisoning by coal-tar products, strychnine and belladonna, for example, do more harm than good, and that small doses may thus prove fatal through the toxicity added to theirs by the supposed antidotes or remedial measures.

Case of poisoning in a man of 29 years after taking within three hours three powders containing each 2½ grains of acetanilide. It proved fatal notwithstanding the use of 1/20 grain of strychnine (with 1/60 grain atropine sulphate) repeated in less than two hours with 1/50 grain digitalin and 1/100 grain nitroglycerin, all given subcutaneously, besides 20 drops of spirit of camphor and a teaspoonful of whisky every hour and a hot pack, with feet elevated, and cold to the head. The terminal symptoms were deep cyanosis, a very weak pulse, a convulsion lasting ten minutes, and pulmonary edema, the latter being verified at the autopsy. A. L. Smedley (Jour. Amer. Med. Assoc., Apr. 27, 1907).

[It is a question whether large doses of strychnine usually given are not more harmful than beneficial in these cases. It raises powerfully the blood-pressure by exciting the vasomotor center. It would thus prove helpful by forcing arterial blood from the deep trunks through the arterioles into the cyanotic tissues were it not that, as is the case with ergot, the arterioles, owing to their diminutive caliber, are the most affected by the vasomotor constriction. In other words, a slight constriction hardly influences a large vessel, while the same degree of constriction will practically close up a very small one. Edema of the lungs may occur under these circumstances simply because the venous stream is itself blocked (being unable to enter the arterial system) by arrest of the arterial circulation, through the excessive constriction of the arterioles. C. E. DE M. S.]

When a large dose is taken, the symptoms once started may suddenly assume marked severity.

Case in a man 52 years of age who suffered from severe chronic headache. Not obtaining relief from headache pills and powders he purchased an ounce of acetanilide in bulk and took a half-tea-

spoonful—about 30 grains. The headache disappeared in a short time, and he then went out on the street. While walking he felt weak. He then went to a barber shop, and the man who shaved him noted that he had a "terrible blueness." He then entered a store, where in a few minutes he was seen to sway and fall to the floor. He was found in deep syncope, extremely cyanotic, with a feeble and rapid pulse. He was readily resuscitated, but in a few minutes there was another attack of syncope, which was repeated a number of times during the next few hours. He gradually recovered. J. B. Tyrrell (Jour. Amer. Med. Assoc., Mar. 31, 1906).

Poisoning by Absorption.—Acetanilide having been recommended as a dressing for wounds, burns, and superficial injuries in general, many cases of poisoning have occurred owing to the large quantities applied to the lesions, and the ease with which it is absorbed.

Two cases also emphasizing the necessity of caution even when using acetanilide externally. The first case had sustained an extensive burn of the left lower extremity. The raw surface was covered with Thiersch's skin grafts taken from the right leg and thigh. An assistant dressed the right limb. Early the next morning the patient became cyanotic, collapsed, and became unconscious. It was learned that the right leg had been copiously dusted with acetanilide. This drug has no place in aseptic cases, while in septic cases more efficient and less dangerous agents are available. F. T. Stewart (Phila. Med. Jour.; Merck's Archives, March, 1902).

Two cases of acetanilide poisoning from absorption from external wounds in children. The first patient was a baby six weeks old who had a troublesome eczema of the buttocks. A powder was applied composed of equal parts of acetanilide and subgallate of bismuth. Twenty-four hours later the skin of the child was markedly cyanotic, the temperature was subnormal, the respirations were feeble and shallow, the pupils were dilated, the heart was rapid and weak, and extremities cold. **Hot applications** were ordered, with the internal administration of **whisky**, and at the end of three days all symptoms of poisoning had disappeared.

A second case was that of a child of two and one-half years who had received a severe scald of the buttocks. A powder composed of equal parts of subnitrate of bismuth and acetanilide was applied, which soon relieved the pain. On the second day the lips, ears, and finger-tips were blue. The symptoms of prostration were present as in the first case, but not to the same degree. The blueness gradually disappeared, and at the end of a week the wound was healed. J. L. Menasses (Inter. Med. Mag., May, 1901).

Case of a woman, aged 37, who for the last eleven months had applied acetanilide powder twice daily to a large and deep varicose ulcer on the leg. She had concealed the existence of this ulcer from her attending physician, and applied the powder to it upon the advice of a friend. Her illness had begun eleven months before with an attack of influenza, which was followed by "indigestion and kidney trouble." She then became troubled with nervousness, worried about trivial things and complained of headache and dizziness. Later she suffered abdominal pain, dyspnea, nausea and occasionally vomiting. There was marked cyanosis, the conjunctivæ being bluish. The heart-sounds were weak. The spleen and liver were not enlarged. The patient lost seventy pounds in the eleven months. She was sent to the hospital, with a diagnosis of some form of severe anemia. The urine was dark amber. The blood was also dark in color, flowed slowly, and coagulated quickly. Red blood-cells numbered 4,370,000; leucocytes 20,960; hemoglobin 53 per cent. There were 95.2 per cent. polymorphonuclears and 2.8 per cent. lymphocytes. The acetanilide was withdrawn and the patient given **Blaud's pills** and **strychnine**. One week later her color and heart-sounds were greatly improved. Blood-count eleven days after admission showed red cells 6,350,000, leucocytes

9920, hemoglobin 63 per cent., polymorphonuclears 74.2 per cent., and lymphocytes 13.8 per cent. R. M. Goepp (Jour. Amer. Med. Assoc., Aug. 4, 1906).

Treatment of Acute Acetanilide Poisoning.—The physiological action of acetanilide being but imperfectly known, cases of intoxication by this drug are treated on general principles, *i.e.*, by measures thought to counteract the symptoms. Cardiac, respiratory and vasomotor stimulants are therefore recommended. **Ether**, hypodermically, has been most frequently used. **Belladonna** is regarded as the best drug to fulfill the indications; it tends to equalize the blood-pressure, especially when external heat is applied simultaneously. **Brandy, digitalis, strychnine, aromatic spirits of ammonia** and inhalations of **oxygen** have all been recommended. **Artificial respiration** is a valuable adjuvant to any treatment adopted.

[In the light of my views, the toxic phenomena being all due to excitation of the sympathetic center, agents which depress this center are indicated. *Amyl nitrite* inhalations, sustained by *nitroglycerin* internally or hypodermically, fulfill this rôle. Artificial respiration is important to insure prompt oxygenation of the blood as soon as the circulation is re-established. Warm (110° F.) *saline solution* intravenously, or, in less urgent cases, per rectum, facilitates excretion of the poison and prevents its irritating action on the sympathetic center, thereby hastening recovery.

Contraindicated.—*Digitalis,* which, like acetanilide, though less actively, excites the sympathetic center, and *alcohol,* which, by becoming oxidized in the blood, favors its conversion into venous blood, and, therefore, cyanosis. *Large doses of strychnine,* which, by causing excessive vasoconstriction, tend to increase the constriction of the arterioles caused by the poison. C. E. DE M. S.]

CHRONIC ACETANILIDE POISONING.—The symptoms of this condition are: cyanosis, which may be extreme, anemia and wasting. The anemia may be of sudden onset and is evidenced by a distinct leucocytosis, marked reduction in the hemoglobin percentage and in the number of red corpuscles, some of which show nuclei. Other common symptoms include disordered digestion, enlargement of the spleen without tenderness, prostration, weak and frequent pulse, dyspnea, excitability, tremor, and mental aberration, with a tendency to deceive in denying the use of the drug. The urine is dark-colored. The combination of warm extremities with marked cyanosis is considered a distinguishing feature of poisoning by acetanilide.

The blood changes above mentioned may not be accompanied by marked impairment of health. Experiments in animals have shown that the prolonged use of acetanilide tends to cause fatty degeneration of the heart, liver, and kidneys.

[The continuous use of acetanilide by perpetuating the irritability of the sympathetic center, and the resulting constriction of the arterioles as explained in preceding commentaries, accounts for the cutaneous ischemia, the cyanosis, the general prostration, and for the rapid and feeble heart action. The decrease of red corpuscles is due to two factors: (1) breaking of the hemoglobin of what corpuscles reach the tissues owing to the deoxidizing power of the latter *(vide supra),* and (2) the rapid conversion, on this account, of normal corpuscles into worn-out cells. This in turn creates a need for an excess of phagocytes; hence the leucocytosis, the methemoglobinemia and the immature red corpuscles. C. E. DE M. S.]

Case in which the most striking point was the good general condition of the patient. Despite the intense cyanosis and the easily demonstrable methemo-

globinemia, he felt and seemed practically well during the intervals of freedom from pain. His headache tortured him, but the methemoglobinemia gave him no inconvenience whatsoever. There was no disturbance of respiration, circulation or any other symptom, if we except the slight evidences of renal irritation which were present from time to time. R. C. Cabot (Phila. Med. Jour., Nov. 29, 1902).

Case of a woman who was extremely nervous, the symptoms accompanying an artificial menopause brought about by the removal of the ovaries for persistent dysmenorrhea. She began by taking an acetanilide proprietary remedy for ovarian pain, and soon drifted to acetanilide because it was cheaper. She had frequent convulsive attacks, which were of a character that led to the diagnosis of uremia. The heart's action was weak and irregular; the mucous membrane of the mouth of the vagina blue; the skin and conjunctivæ were white. The urine had a low specific gravity and a large quantity of albumin. A large amount of acetanilide was found in the patient's trunk. This being taken away, she soon manifested the peculiar traits characteristic of drug habitués. She used every possible means to obtain the drug. With watching, rest, and tonics, she soon began to improve, and in six months was perfectly well. Since the recovery there has been no inclination to return to the habit. The clinical picture in this case was almost typical of the advanced stages of parenchymatous nephritis. T. W. Luce (Amer. Med., Sept. 26, 1903).

In a considerable number of cases of chronic acetanilide poisoning studied, the blood picture was quite characteristic. The hemoglobin cannot be estimated, on account of the presence of methemoglobin, which gives the characteristic chocolate color to the blood. The red cells are usually reduced in number and are more or less deformed. There is usually leucocytosis.

In cases of severe chronic poisoning by acetanilide and related coal-tar products, the symptoms are usually very similar as concerns progressive mental and physical debility, which later often reaches a high grade. There is cardiac weakness, with more or less pronounced cyanosis. Apart from the usual chocolate hue of the blood so noticeable on puncture, the blood picture, were it not for an almost invariably present leucocytosis, would suggest pernicious anemia. D. D. Stewart (Jour. Amer. Med. Assoc., June 3, 1905).

Case of a man, 38 years old, merchant, who consulted the author on account of increasing weakness, nervousness, and shortness of breath. At times he suffered from palpitation of the heart and throbbing in the neck. There was blueness of the lips, face, and finger-nails. There was a history of neuralgia. Heart slightly enlarged. No murmurs. The urine showed indican in considerable quantities. The blood was practically normal, with the exception of a constant polycythemia (6,000,000 red blood count). At first the patient would not admit taking any drug, though later he confessed having used a patented headache powder for some months. Withdrawal of the drug and general tonic treatment restored him to health in about six months.

Case of a woman, 27 years old, resembling first case closely. Here the red blood count was always under four millions. Stengel (Jour. Amer. Med. Assoc., July 22, 1905).

The almost constant manifestation of chronic acetanilide poisoning: (1) cyanosis that may be extreme; (2) more or less dyspnea and general weakness, and (3) dark-colored urine that contains paramidophenol and an increased amount of the ethereal sulphates. A most striking and characteristic condition is the anemia of the secondary type with degenerate and nucleated red corpuscles. Methemoglobin may be present in the blood and in the urine. Dizziness, syncopal attacks, tinnitus, palpitation, may be pronounced where the anemia is advanced. The spleen is often enlarged. Anorexia, nausea, vomiting, and diarrhea may occur. Nervousness and restlessness are aggravated by the removal of the drug, to which the patient has become habituated. J. B.

Herrick and E. E. Irons (Jour. Amer. Med. Assoc., Feb. 3, 1906).

Case of a young woman who had persisted in taking some coal-tar product originally prescribed for migraine. About a year after her marriage she died suddenly following an apparently normal labor. The knowledge of the continued use of the prescription during pregnancy gave the clue to the cause of death. A great danger of chronic poisoning with coal-tar products is the sudden yielding of the heart to unusual strain. S. Solis-Cohen (Boston Med. and Surg. Jour., Feb. 22, 1906).

Case of chronic acetanilide poisoning. The patient had long used acetanilide, about a dozen 5-grain tablets in twelve hours. She procured 1000 at a time, and in four years had used several thousand. She suffered from severe headaches and vomiting attacks lasting for two or three days, and, as a rule, she would have to be in bed. Two years earlier she began the use of morphine together with the acetanilide and was using as much as 2 grains of morphine a day to get relief. When first seen, she had been in bed for six weeks, was emaciated, no appetite on account of persistent vomiting, headache always present; slightly jaundiced, with marked tenderness and dullness over the gall-bladder region; very constipated, and suffering from tympanites. Dr. A. F. Jonas drained the gall-bladder of dark, thick, stringy bile. She made a good recovery from the effects of the operation, and in three weeks was up and around a little. She stopped the use of any drug and in a couple of months was doing her work and feeling well. About a year and a half later suffered from headache, vertigo, faintness, tinnitus, psychic irritability, dyspnea, palpitation, and edema, with tenderness over the gall-bladder region; large quantities of bile and mucus were being vomited. She was using coal-tar products and morphine to relieve the pain. Her lips and finger-nails were blue. She had lost about 20 pounds in weight during 4 to 6 weeks. Overgaard (Western Med. Rev., March, 1911).

Treatment of Chronic Acetanilide Poisoning.—Under the gradual withdrawal of the drug, **strychnine** and **digitalis**, these cases usually recover promptly. If pains and insomnia occur, **codeine** may be used tentatively lest another evil habit be initiated. Constipation, which is apt to follow for a time, should be counteracted by **saline aperients.** Sympathy and encouragement are potent factors for good in these cases.

[Here both **strychnine** and **digitalis** are effective because they counteract not the direct action of the acetanilide on the sympathetic center, but the exhaustion of this center. *Codeine* or *morphine,* administered with due caution, are effective in counteracting this exhaustion, since they also act—from my viewpoint—mainly by exciting the same center. C. E. DE M. S.]

The acetanilide—and this applies to all coal-tar analgesics—habit is much more easily recovered from than the opium and morphine habits, and offers, therefore, in this respect a marked advantage over the latter.

> The treatment is comparatively simple. With gradual withdrawal of the drug, the temporary substitution of **codeine** to relieve pain, and the use of **tonics** and attention to the stomach and bowels, recovery will usually ensue. Watchfulness against relapse is necessary, but the habit has not usually as strong a hold on the patient as morphine or cocaine. Even in the worst cases a hopeful prognosis can usually be given. J. B. Herrick and E. E. Irons (Jour. Amer. Med. Assoc., Feb. 3, 1906).
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> Case of a man, aged about 26, under treatment for two years for syphilis, who had taken enormous doses of the iodides. He had suffered greatly from headache and showed an obscure and progressive tendency to cyanosis. The character of the latter, with the cardiac symptoms and splenic enlargement, led to the diagnosis of acetanilide poisoning. It was

learned that the patient had had migraine previous to the specific infection and formed the habit of taking various headache powders. Lately he had been using from six to twenty "orangeine" powders daily. Attempts to withdraw the drug being followed by intense headache, small doses of **morphine** were substituted without the patient's knowledge. All the symptoms disappeared and the patient left the hospital without having taken either acetanilide or morphine for two or three weeks and without the knowledge that he had had the latter. The headache did not return. J. C. Wilson (Boston Med. and Surg. Jour., Feb. 22, 1906).

APPLIED THERAPEUTICS OF ACETANILIDE.—There is no ordinary acute febrile state (the temperature remaining below 105.5° F.) in which the use of acetanilide as an antipyretic is warranted. In typhoid fever, for example, it causes, as shown above, and even when given in very small doses, marked depression tending to collapse. It favors in no way the curative process, and the more or less sudden fall produced deprives the clinician of an important danger-signal which points to intestinal hemorrhage, and thus prevents the utilization of measures calculated to arrest it. The comfort acetanilide brings to the patient is the treacherous and insidious dulling of all sensations many poisons afford; it may be procured quite as effectively and with benefit to the patient by means of cold baths, cool sponging, etc., by abstracting heat. Acetanilide does not shorten the course of fevers, does not prevent complications nor reduce the mortality. The same reasons that prevail against its use in febrile processes cause acetanilide to be contraindicated in phthisis. It has been used to counteract the afternoon rise of temperature, but the advantage gained is more than offset by the depression produced. Ten grains in divided doses have produced collapse.

Most authorities, however, advocate the use of acetanilide or other antipyretics of the coal-tar series when the temperature is sufficiently high to endanger life, *i.e.*, in **hyperpyrexia.**

[Acetanilide is not a true antipyretic. By causing constriction of the arterioles it merely reduces the volume of blood admitted into the tissue-capillaries and causes it to accumulate in the deep vascular trunks. It does not stay the progress of the disease, but tends to interfere with the curative process by preventing the free access of the antitoxic and bactericidal substances to the diseased area.

Acetanilide is not even valuable in hyperthermia, since it does not diminish in the least the excessive production of antibodies to which the hemolysis and autolysis are due. Thus, Schütze (Zeit. f. Hygiene, Bd. xxxviii, S. 205, 1901) and Beniasch (Zeit. f. klin. Med., Bd. xlv, S. 51,'1902) have both found that the proportion of protective antibodies in the blood is not modified by coal-tar antipyretics, the agglutinating properties being in no way diminished, even when very large doses were given to infected animals. The destructive process is merely transferred to the deeper vessels. As previously stated, therefore, excessively high temperature (above 105.5° F.) or a temperature sufficiently high to produce discomfort is best treated by means of hydrotherapeutic methods, especially cool sponging. C. E. DE M. S.]

It is in the diseases of the nervous system that acetanilide has shown itself most valuable. As an analgesic, especially in cases of **neuralgia** or **neuritis,** or in pain from reflex causes, acetanilide has been of marked benefit. In **sciatica, migraine, intercostal neuralgia, gastralgia,** the pain of **optic neuritis** and **glaucoma,** it has been freely used, and still maintains a well-deserved reputation. It is also effect-

ive in the neuralgic pains associated with **herpes zoster.**

[Whichever of the many causes of these disorders prevails, the pain is always due, as shown elsewhere ("Internal Secretions," vol. ii, p. 1529), to engorgement of the minute vessels, the vasa nervorum, that supply blood to nerves, and the pressure they exert upon the nervi nervorum, which, as shown by Horsley, terminate in minute sensory bulbs. Acetanilide, by causing constriction of the arterioles which supply these neural vessels, diminishes their hyperemia, and thereby arrests the pain.

In some cases, especially when full doses of acetanilide cannot be given, the neural hyperemia is further counteracted by giving sodium bromide (10 or 15 grains) or nitroglycerin (1/100 grain) or again spirit of nitrous ether (½ to 1 dram) with each dose. All three agents, by causing general vasodilation, cause the blood to accumulate in the deeper vessels, and thus to deplete those of the periphery, including the vessels of the painful nerves.

In sciatica, acetanilide is aided by sodium salicylate, which, besides causing constriction of the arterioles, also promotes the destruction of toxic wastes, the underlying cause of the sciatica. The doses of both agents should be small, however, to avoid undue constriction of the cardiac arterioles, and the resulting depression. C. E. DE M. S.]

All headaches that are severe or long-continued or of regular recurrence should be carefully studied and the causative disorder treated. The most satisfactory temporary treatment in the author's experience has been the following, varied according to age and other conditions:—

℞ *Acetanilidi* ..... ʒj (4.000).
Sodii bromidi ..... ʒij (8.000).
Caffeinæ citratæ ..... gr. iv (0.250).
Elix. guaranæ..q. s. ad ʒij (60.000).

One teaspoonful every three hours for headache. E. M. Alger (Therap. Gaz., Dec., 1903).

The **painful menstruation,** especially in young girls, **ovarian pain** and the circulatory and nervous disturbances occurring at the **menopause** often yield to it. It has been used with benefit **in chorea.**

[The manner in which acetanilide relieves pain in menstrual disorders, etc., is similar to that in neuralgia.

In chorea, it is the hyperemia of the cerebrospinal and muscular systems which underlies the choreic movements that is reduced by acetanilide. This drug sometimes proves a valuable adjuvant, moreover, to remedies addressed to the cause of the disorders. S.]

In the **lightning and girdle pains of tabes,** acetanilide has been found very effective by Lépine, Grasset, Hayem and others. But 10-grain (0.66 Gm.) doses are required. These subdue the suffering in one-half hour and can be renewed when necessary.

[This is produced in the same way, the pains being due mainly to hyperemia of the central and peripheral nervous elements, including the nervi nervorum. C. E. DE M. S.]

In **epilepsy,** acetanilide has, on the whole, not shown itself very useful, except in cases characterized by permanently high vascular tension. At best, however, it serves but to defer the paroxysms. This applies also to **tetanus.**

[The spasms, interpreted from my standpoint, are caused by toxic wastes, which, by exciting the vasomotor center, produce an intense rise of blood-pressure and hyperemia of the cerebrospinal system. By contracting the arterioles, acetanilide counteracts this hyperemia, but, of course, only temporarily, and thus reduces the number of convulsions in a given time. It is, however, at best, a palliative. C. E. DE M. S.]

Vomiting of nervous origin or due to marked gastric irritability occasionally yields to its action. Two grains every hour until 6 grains have been taken usually suffice to arrest this morbid symptom. It gives some relief **in seasickness** in doses of 3 to 5 grains (0.20 to 0.32 Gm.).

In **pertussis,** acetanilide has been found to lessen the paroxysms markedly. It can be given in doses of ¼

to ½ grain (0.016 to 0.032 Gm.) in small children.

[Pertussis, from my viewpoint ("Internal Secretions," vol. ii, p. 1716), is due to irritation of the sensory terminals of the respiratory tract by a pathogenic agent of unknown identity. Acetanilide, by causing constriction of the arterioles, reduces the blood supplied to the terminals, and markedly reduces the reflex cough they provoke. C. E. DE M. S.]

Acetanilide has been used with advantage in **influenza**. But, as antipyrine and acetphenetidin are quite as effective and less prone to produce untoward effect, they should be given the preference.

Increased comfort to the patient and occasionally general improvement have been secured by the use of acetanilide in **diabetes mellitus**.

[In this condition the cutaneous irritation, especially the pruritus, is often a source of considerable suffering. Acetanilide, by causing constriction of the cutaneous arterioles and thus diminishing the hyperemia, affords considerable relief. Moreover, it tends directly to counteract the morbid process itself by inhibiting in the same way the functions of the adrenals, which (see "Internal Secretions," p. 1583) are overactive in this disease. The drug is valuable, however, only in sthenic cases and should be avoided when the disease is advanced. C. E. DE M. S.]

In ordinary **myalgias**, especially **lumbago**, acetanilide proves sometimes very effective. It relieves not only the pain, but also the stiffness. It has likewise been recommended in **acute articular rheumatism**, especially when the pain and swelling are marked. It should not be given when **cardiac complications** are present. Doses of 5 grains (0.3 Gm.) not oftener than three times daily usually suffice.

[From my viewpoint this form of rheumatism is due (see "Internal Secretions," vol. ii, p. 1868) to capillary hyperemia. The beneficial action of acetanilide is the result, therefore, of diminution of the volume of blood admitted into these vessels. The following combination has been found efficacious in cases which had resisted the action of salicylates:—

℞ *Acetanilidi* ..... gr. xxiv (1.6 Gm.).
Camphoræ monobrom. gr. xij (0.8 Gm.).
M. et div. in capsulæ no. xij.
Sig.: One every three hours three times, then every four hours. C. E. DE M. S.]

Harnsberger found the drug useful in threatened **abortion** and in **habitual miscarriages**.

[Abortion is often due to congestion of the uterus. Hence the beneficial action of acetanilide in certain cases. By causing contraction of its arterioles, it is also useful in all cases to arrest the hemorrhage. C. E. DE M. S.]

The drug is sometimes used internally in the treatment of **coryza**. In **pharyngeal irritation** and inflammation it is effective internally, especially when aided by a gargle of 4 grains (0.25 Gm.) to the ounce (30 c.c.) of water. Insufflations of acetanilide are very useful in **tonsillitis**.

[As these are all catarrhal processes in which hyperemia is the main morbid condition, the mode of action of acetanilide is self-evident. C. E. DE M. S.]

LOCAL USES.—Acetanilide has been employed with benefit in cutaneous disorders, such as **eczema, psoriasis, urticaria**, and **herpes**, usually in an ointment. It may be used in powder form to dust over the initial lesion of syphilis, **mucous patches**, and **chronic ulcerations**, as well as **chancroids**. It has been employed in injections for the treatment of **urethritis** and **vaginitis**. The proportion of the drug used in ointment or liquid applications is generally from 20 to 40 grains to the ounce. It has been extensively used as an antiseptic and

analgesic in wounds and burns of varying extent, one of its main advantages being lack of odor. It is best used in combination with an equal part of finely divided boric acid.

The *danger* of absorption and poisoning by the drug render its local use unwise, however, in any but minor injuries, and the quantity applied at each dressing should not exceed that of a moderate dose given internally. We have submitted under the heading "Poisoning by Absorption" several illustrative cases.

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ACETIC ACID.—Acetic acid is an organic acid obtained from sugar or wood by distillation, or from ethyl alcohol by oxidation; or again from crude pyroligneous acid. It is also formed normally in the stomach, from sugars and alcohol taken as foods.

PROPERTIES.—Acetic acid is a clear, colorless fluid having a strong pungent odor and an intensely acid corrosive taste. It contains 36 per cent. of glacial acetic acid: a monohydrate presenting the physical properties of acetic acid, which, in turn, becomes crystalline at 34° F.

The *dilute acetic acid* is officially prepared by adding 1 part of acetic acid to 5 of water. Good vinegar corresponds approximately in strength with dilute acetic acid. Each is used as a local astringent, and internally or by inhalation as a stimulant.

Glacial acetic acid is employed as an escharotic. The crystalline form is mainly employed with sulphate of potassium in the preparation of smelling-salts.

Trichloracetic acid prepared by treating acetic acid with chlorine, which occurs in the form of deliquescent crystals, is to be preferred as an escharotic.

USES AND DOSE.—The preparations available are:—

Glacial Acetic Acid (*Acidum Aceticum Glaciale*); escharotic.

Acetic Acid (*Acidum Aceticum*); used externally.

Dilute Acetic Acid (*Acidum Aceticum Dilutum,* 6 per cent.); dose, ½ to 1 dram (2 to 4 c.c.).

Trichloracetic Acid (*Acidum Trichloraccticum);* escharotic.

It is miscible with alcohol or water in all proportions.

PHYSIOLOGICAL ACTION.—Applied to the skin glacial acetic acid caused irritation and pain, and the formation of a vesicle; its local application to mucous membranes is attended by immediate blanching of the cellular elements cauterized. When applied to the skin well diluted, as vinegar, for example, it acts as an astringent and produces cold and pallor of the tissues it touches. Greatly diluted, as a beverage, it quenches thirst. In the blood it combines with the alkaline bases, is transformed into acetates, and then into sodium bicarbonate, and thus acts as a diuretic and diaphoretic.

ACETIC ACID POISONING.—The abuse of vinegar, or vegetables and other foods preserved in this agent, tends to produce anorexia, gastric disorders, diarrhea and emaciation. In toxic doses acetic acid causes intense irritation, owing to its property of effecting a partial solution of albuminous bodies and of dissolving gelatinous tissues. This escharotic action, by manifesting itself upon the mucous membrane of the pharynx and larynx, is

liable to cause edema of the glottis: a danger to be at once thought of. The immediate manifestations are severe pain in the mouth, throat, esophagus, and stomach, with retching and vomiting and other symptoms attending violent irritation of the digestive tract. General symptoms then manifest themselves: The heart's action becomes rapid and the pulse extremely weak or imperceptible, the face and extremities being cold and clammy and covered with sweat. In very acute cases, somnolence passes into coma, and death ensues.

In moderately severe cases, there occurs, after the disappearance of the acute symptoms, abundant expectoration of mucus, containing necrosed tissue, and slight fever, due to more or less pyemia. The blood is markedly influenced, as shown by the marked anemia, paleness and distortion of the red corpuscles and other phenomena. Such a case usually recovers.

[What experimental evidence is available is too scanty to warrant a conclusion as to the manner in which it produces physiological effects. It would seem, however, as if the general phenomena awakened by a toxic dose of acetic acid were reflex in character, the vagus transmitting the afferent or sensory impulses from the cauterized alimentary canal, while the sympathetic carries the efferent or motor impulses to the vessels it supplies, the arterioles. The cardiac arterioles being constricted and the myocardium thus inadequately supplied with blood, the heart's action becomes weak and the pulse-wave likewise. A similar condition prevailing throughout the entire organism the body is cold and clammy, and relaxation of the spiral muscles of the sweat-glands causes passive sweating. A corresponding interference with the circulation of the brain causes somnolence and finally coma.

These general phenomena last during the inflammatory phase of the lesions in the alimentary canal, the seat of reflex excitation. C. E. DE M. S.]

Treatment of Acetic Acid Poisoning.—Alkalies and demulcents should be employed. The **bicarbonate of soda** in free solution is an effective remedy. Ordinary **soap**—one containing an alkali—can be used in solution until an alkaline salt is available. **Chalk, lime** or even **wood ashes** may be employed in the absence of an alkaline soap. **Milk, white of egg, oil** or **flax-seed tea** are useful to form a coating over the esophagus and stomach.

Case of a girl, aged 19 years, who swallowed a considerable amount of strong acetic acid with suicidal intent. She immediately was seized with violent vomiting and with pain and intense burning in the mouth and pharynx. At the hospital she developed a series of pronounced symptoms, which are interesting in view of the rarity of cases of acetic acid poisoning. There was a frequent and feeble pulse and a slightly elevated temperature, a persistent and violent cough with a very abundant purulent expectoration, a veritable bronchorrhea, and occasionally efforts at vomiting which were not successful. The urine was black and smoky, like that of carbolic acid poisoning, and contained 1 per cent. of albumin. The red blood-disks in the fresh blood were very pale, with little tendency to form rouleaux, and with frequent mulberry-shaped distortion. The serum, when separated, had a distinct reddish tint, showing that the hemoglobin had been dissolved from the cells. The heart-sounds and the apex-beat were very weak. The symptoms gradually disappeared, and the patient was discharged cured. The treatment consisted of stimulation in the shape of injections of **caffeine**, a **milk diet**, and the use of pieces of **ice** and of a **tannin** gargle for the throat. Special attention called to the changes in the blood, the purulent bronchitis, and the degenerative changes in the myocardium resulting in heart-weakness with danger of cardiac failure. Giordano (Riforma Medica, Jan. 27, 1904).

To counteract the general symptoms, **strychnine** or **caffeine** may be used. To relieve the burning sensation in the alimentary canal, **morphine** is sometimes used.

THERAPEUTICS.—As an **antiseptic,** acetic acid is possessed of considerable power. As such it may either be applied locally or its fumes may be inhaled.

> In an emergency vinegar is useful for disinfecting the hands and the region operated upon. L. Fürst (Deut. Aerzte-Zeit., June 15, 1900).

Acetic acid is frequently used as a **stimulant.** When inhaled its stimulating effects upon the nervous supply of the nasal mucous membrane causes it to sometimes act rapidly in restoring consciousness after **fainting.** In the same manner it may also arrest **vomiting** and **headaches** of nervous origin.

Acetic acid is useful in many disorders of the skin. As an escharotic it is often used on **corns, warts, condylomata,** and **fungous growths.** The glacial acetic acid should be used for this purpose. For the destruction of **papillomata** and other small growths, the trichloracetic acid is more effective. The neoplasm is first anesthetized with cocaine, and a single crystal of the acid is placed upon it. This produces a white, dry mass which falls off. In **alopecia** it has been used with advantage as a vesicant. When it is extensive the scalp should be shaved and dilute acetic acid with equal parts of chloroform and ether applied. Or Besnier's formula may be employed:—

℞ *Chlorali hydrati* ..... 75 grs.
Ætheris ..... 6 drs.
Acidi acetici cryst...... 15-75 grs.

Misce. These applications are repeated two or three times a week at first, and later at longer intervals.

Between times a stimulating oil—as of eucalyptus and turpentine, of each ½ ounce; crude petroleum and alcohol, of each 1 ounce—is applied. This is to be followed by a thorough massage of the scalp for five minutes by the patient. Once a week, or oftener, the scalp is to be thoroughly shampooed with tincture of green soap (Morrow).

In **rodent ulcer** and **lupus vulgaris** acetic acid is of use. Daily applications of a 75 per cent. solution and subsequent rinsing with water are necessary.

In **sunburn** and the various forms of **dermatitis** dilute acetic acid or vinegar limits greatly the cutaneous hyperemia, the main source of discomfort.

Acute coryza is sometimes arrested by the inhalation of acetic acid. This applies also to **epistaxis;** in persistent cases, a tablespoonful of vinegar in a glassful of water hastens materially the beneficial effect inhalations afford.

Glacial acetic acid is useful in preventing the development of **hay fever** by applications after local anesthesia with a 10 per cent. solution of cocaine to sensitive areas of the nasal mucous membrane twice per week. In practically all cases, however, the applications must be renewed each year. In **hypertrophic rhinitis** it may also be used in the same way; but chromic acid is more effective. In **pharyngitis** and **tonsillitis** gargling with equal parts of vinegar or dilute acetic acid and water sometimes proves very efficient.

In **tuberculous laryngitis** it has given good results in arresting ulceration. The ulcers are first scraped and the acid applied with a laryngeal applicator. Inhalations of a 2- to 3-per cent. solution three times a day, ten minutes at a time, and continued several weeks, have been recommended by several German observers.

Acetic acid has also been found an excellent adjuvant in the treatment of **pulmonary tuberculosis** and **bronchitis** when used every three hours. A convenient method is to pour about a teaspoonful on a saucer and to place this over a fire. The acid is then inhaled while it is evaporating—about ten minutes. At first it proves irritating, but this soon subsides. It is useful in **night-sweats** applied as a lotion. Vinegar half diluted with water is quite as effective.

Diluted with from one to four parts of water, dilute acetic acid is recommended by Wood in **hematemesis.** It has been recommended by Hayem for **dyspepsia,** especially where the digestive activity is deficient, *i.e.,* in hypopepsia.

It is a good succedaneum for hydrochloric acid in the treatment of **gastric** and **acute** or **chronic intestinal catarrh,** ordinary vinegar, a tablespoonful to half a pint of water, being taken daily. It is indicated in those submitted to a diet rich in carbohydrates and unable to take much exercise. It also controls **summer diarrhea** and **true cholera nostras,** vinegar rapidly and certainly killing the bacillus of cholera.

Inhalations of acetic acid are very effective in the **vomiting of chloroform narcosis,** administered as in the "drop" method of anesthesia, the napkin being held near the nose, but not in contact with the tissues.

Dilute acetic acid or vinegar is efficient as a topical application for **sprains** and **bruises** and reduces greatly the effusion and pain.

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ACETONE BROMOFORM.

See Bromine.

ACETONE CHLOROFORM.

See Chloretone.

ACETONURIA. — Acetone (C_3H_6O = dimethylketone = CH_3—CO—CH_3) is a thin, watery, very mobile, colorless liquid of neutral reaction. It has a curious aromatic odor, resembling somewhat that of acetic ether or of oil of peppermint. It is soluble in water, in alcohol and ether in all proportions; evaporates at ordinary temperatures; boils at 56.3° C., and has a specific gravity of 0.81. Acetone can be obtained by the distillation of acetate of barium. Oxidation of acetone causes the formation of acetic acid and formic acid. As a product of metabolism, it was discovered by Petters, in 1857, in the urine of a diabetic patient.

Acetone is found in the urine of healthy individuals in quantities not exceeding 10 mg. per day, which, during starvation (Müller), can increase to 780 mg. per day. In some diseases it increases to 0.2 to 0.5 gram daily. By distilling the urine examined, acetone can be obtained in a purer state, although still united with other volatile constituents of the urine.

PHYSIOLOGICAL AND PATHOLOGICAL EXCRETION OF ACETONE. — Pathological acetonuria is observed (1) in high febrile states; (2) in diabetes, especially in advanced cases; (3) in some forms of carcinoma which have not as yet induced inanition; (4) in psychoses; (5) in autointoxication; (6) in functional insufficiency of the pancreas; (7) during the excessive use of animal foods, and (8) in different disorders of the digestion. Lorenz observed

acetonuria and excretion of acetone with the feces and the vomited matter in a case of peritonitis. In fever acetonuria is constantly observed, and in the fevers of children as well (Baginsky). In cases of diabetes, acetonuria occurs when the disease has continued for a long time, and especially when the patients are put on an exclusive diet of proteids or proteids and fat, or when the allowance of food is not sufficient to maintain the equilibrium of metabolism.

In fevers, as well as in diabetes, acetonuria is often accompanied by excretion of diacetic acid and beta-oxybutyric acid.

Five cases of gastric disturbances accompanied by elimination of acetone and acetic acid; the breath had the peculiar odor of acetone at times. Only a few of the children had fever during these attacks. The children were between 3 and 11 years old. The writer ascribes the vomiting to efforts at elimination. Hecker (Münch. med. Woch., July 14, 1908).

The presence of acetonuria seems to possess some diagnostic value in differentiating between diphtheria and scarlet fever, on the one hand, and an ordinary sore throat, on the other. It is much more constantly present in the former cases. In adults, even in diphtheria and scarlet fever, it is not present so constantly as in children.

Of 197 consecutive cases of scarlet fever admitted into the Isolation Hospital, Southampton, 167 were found to have acetonuria, which is equal to a percentage of 84.8. Of 96 cases of diphtheria 87 were found to have acetonuria, which is equal to a percentage of 90.6. Of the adults admitted 8 had acetonuria and 7 had none. There were only 2 cases of diphtheria in children in which no acetone was found; 1 of these cases was one of laryngeal diphtheria in which the toxic symptoms of diphtheria are generally absent. Of 21 cases of enteric fever only 7 showed some evidence of acetonuria, which is equal to a percentage of 33.3. In 6 of these 7 cases the acetonuria was so slight as to be only with difficulty demonstrated. Of the 14 cases that had no acetone in the urine 8 were severe cases. Alfred Harris (Lancet, May 14, 1910).

Case of periodical vomiting and acetonuria in a child. The patient was a boy of about 3, much depressed by the periodical vomiting. The odor of acetone permeated the air of the room. He had seven attacks of the recurring vomiting, each accompanied by much acetonuria, during the two years afterward, but then he seemed to outgrow the tendency and is now an apparently healthy child. Adenoid vegetations had been removed in the interim. Bloch (Hospitalstidende, June 8, 1910).

It occurs also in association with typhus, pneumonia, variola, scarlet fever, perityphlitis, Bright's disease and strangulated hernia, but it does not lead in such cases to diabetic coma.

Case of autointoxication with acetonuria and bradycardia. The pulse registered from 4 to 8 to the minute and was synchronous with the heart beat. This shows the extreme grade of the intoxication of the inhibitory vital centers and of the myocardial degeneration. There was a leucocytosis of 22,000. Two separate and distinct toxemias were present: a clear history of chronic nicotine poisoning and an acute infection. Singer (N. Y. Med. Jour., June 26, 1909).

Costa found during the last month of physiological pregnancy and in the puerperium (after the eighth day) a more marked acetonuria than in the non-pregnant state. In labor the acetonuria increases. Acetonuria cannot be regarded as a sign of fetal death.

Twenty-six cases of acetonuria studied. In physiological pregnancy at the ninth month the acetonuria is more marked than in the non-pregnant state.

In labor the acetonuria increases, especially if the parturition be prolonged. In the puerperium it diminishes, remaining, however, greater than in pregnancy till after the sixth day. The view that acetonuria can be regarded as a sign of fetal death is not sustained. R. Costa (Ann. di Ostet. e Gynec., xxiii, March, 1901).

ORIGIN AND PATHOLOGICAL SIGNIFICANCE OF ACETONE, DIACETIC ACID, AND BETA-OXYBUTYRIC ACID.—The origin of acetone in the organism has not yet been ascertained. Cantani was of the opinion that it was formed in functional disorders of the digestive tract; Petters and Kaulich argued that it was due to fermentations in the bowels. Markownikoff ascribed it to a fermentative product of sugar.

Albertoni did not find acetone in the urine of animals which had received large doses of glucose (100 grams) or of different primary saturated alcohol; when isopropylalcohol was ingested it was excreted partly unaltered and partly changed to acetone, and when acetone was given to animals it was discharged by the urine, even if the dose of acetone ingested did not exceed 8 cg.

When Gerhard detected the presence in the urine of a substance which gave a dark wine-red color by means of a solution of perchloride of iron, he believed this substance to be diacetic ether, and was of the opinion that acetone was derived from this substance, which can easily be disintegrated into acetone, alcohol, and carbonic acid.

Fleischer and Tollens then demonstrated that Gerhard's view was erroneous, and found that the coloring substance—at least in the majority of cases—must be diacetic acid, which can be separated from the urine by the addition of sulphuric acid and extracted with ether. This opinion is supported by von Jaksch. Minkowski caused acetonuria by extirpation of the pancreas, and von Mering by intoxication with phloridzin.

Lustig found that extirpation of the solar plexus in animals provoked acetonuria, glycosuria, and emaciation, while Oddi obtained the same results by sugar injections.

Lorenz is of the opinion that diacetic acid and the beta-oxybutyric acid are the substances from which acetone is derived, and that they are the real causes of the toxic symptoms observed in acetonuria, while acetone itself is relatively innocuous.

The necessary condition for the production of acetonuria is an insufficient decomposition of hydrocarbons, either from their absence in the diet or from impaired powers of decomposition on the part of the organism (diabetes). In advanced diabetes acetonuria is a grave symptom, threatening coma. This coma may be delayed by the administration of large doses of sodium bicarbonate. It is probable that the bodies of the acetone series are formed in considerable quantity in the organism, to disappear completely later. They doubtless represent links in a continuous series of transformations in which oxybutyric acid-beta is the primordial term. H. C. Geelmuyden (Norsk Mag. f. Laegevidensk., July, 1900).

Brewer, Brackett, Stone and Low have held that acetonuria is fairly rare and that it is of unfavorable significance. The writer cannot agree with these views. His own conclusions are: 1. Acetonuria is of more frequent occurrence than is thought. 2. Its presence without symptoms has no effect on operative treatment or prognosis. 3. Its presence with moderate symptoms is of only slight importance. 4. Its presence with severe symptoms, however, is of the gravest prognostic value. Hubbard (Boston Med. and Surg. Jour., June 29, 1905).

According to Geelmuyden, the necessary condition for the production of acetonuria is an insufficient decomposition of carbohydrates; he thinks it probable that the bodies of the acetone series are formed in considerable quantity in the organism, to disappear later.

Hubbard found acetonuria more frequent than is generally believed. Its presence without symptoms should not influence operative treatment or prognosis. While its presence with moderate symptoms is of but slight importance, its presence with severe symptoms renders the prognosis very grave.

Von Engel found a great quantity of acetone in the urine of a patient suffering from lactosuria; when the milk was removed by a sucking apparatus the acetonuria disappeared. Very much acetone was found in the urine of patients suffering from severe chronic morphinism. In different acute fevers acetonuria is rather a constant symptom; in typhoid fever von Engel found it constantly; acetone was only missed when the typhoid fever was accompanied by obstipation.

Becker found that acetonuria increased after narcosis, the case being the same with an already existing acetonuria. This would seem to explain why acetonuria has been observed after great operations.

> Etherization itself will produce acetonuria in a certain number of cases, but it also seems very probable that there are a good many other contributing factors which must be taken into consideration, such, for example, as prolonged starvation before and after operation. In a large series of observations made in a children's hospital it was found that boys were more subject to postanesthetic acetonuria than girls. The length of the anesthesia, the amount administered, and the duration of the operation seem to play no part in the duration and severity of the symptoms, but the method of administration of the ether seems to be of considerable importance, as a comparison of figures will show. In 120 cases etherized by the "cone method," acetone was found in 88.5 per cent., while, in the same number of cases in which the drop method was used, only 26 per cent. showed acetonuria. It would, therefore, seem perfectly logical to consider the "drop method" the best. Hamblen (Univ. of Penna. Med. Bull., June, 1909).

Beesly, Longo, Young and Williams found postoperative acetonuria a quite common occurrence (70 per cent.). The condition is transient, lasting only from two to eight days (Young and Williams). Acetonuria has no influence upon the course of the recovery. Beesly holds that acetonuria due to chloroform anesthesia is more harmful than that caused by ether anesthesia, because ether is less injurious to the hepatic and renal cells and thus does not inhibit their power to carry on their eliminative functions.

The usual risks of anesthesia are not increased by pre-existent chronic acetonuria, but anesthesia (especially by chloroform) may be dangerous with pre-existent acute acetonuria.

> In postanesthesic acetonuria two separate conditions should be recognized —acute and chronic acetonuria. Ether and chloroform invariably induce a temporary acute acetonuria which may be very detrimental, even to an apparently healthy organism. This acute anesthetic acetonuria is accompanied by symptoms of acid intoxication, sometimes ending in death, when the kidneys are unable to cope with the increased formation of acetone by a corresponding incapability of excretion. Although ether may produce a greater acetonuria, this is less harmful than that produced by chloroform, because ether is less injurious to the cells of

the liver and kidneys, and thus does not hinder their power of elimination. The more plentifully and rapidly excretion is carried on, the less serious is the poisoning. The effects of the poisoning are mitigated by the administration of alkalies, which may also be given with advantage before operation if poisoning be anticipated.

The usual risks of anesthesia are not increased by pre-existent chronic acetonuria. Anesthesia is dangerous with pre-existent acute acetonuria, especially if the anesthetic is chloroform. A guarded prognosis must always be given when acute acetonuria is present with symptoms of poisoning. Death following the administration of chloroform with symptoms of poisoning may be due to the idiosyncrasy of the patient. Lewis Beesly (British Medical Journal, May 19, 1906).

Study of 102 cases with reference to the presence of acetone in the urine after operations. The writer found acetone absent in 76; present in 11 cases before the operations, and absent in 15; present in 86 cases after the interventions. Postoperative acetonuria is therefore a quite common occurrence. The condition is transient, and is caused by both the anesthesia and the traumatism. Youth and fasting are predisposing factors. The acetonuria has no influence upon the course of the postoperative recovery. Longo (Riforma Medica, Sept. 15, 1907).

The writers have made some observations in 52 cases, of whom only 2, or about 3.8 per cent., had acetonuria before operation, while following laparotomy acetone was found in the urine of 27, or about 52 per cent. The reaction lasted in different cases from two to eight days. Of the 2 patients whose urine contained acetone before operation, 1 was a colored girl, 15 years of age, who was operated upon for adhesions following an acute attack of pelvic inflammation. The operation was short and the convalescence excellent. Young and Williams (Boston Med. and Surg. Jour., Jan. 23, 1908).

Acetone, diacetic acid, and beta-oxybutyric acid are found in great quantities in the urine of diabetic coma, and different authors—Munser and Strassez, for instance—believe these substances to be the real cause of coma, perhaps by causing an excess of acidity in the organism.

In comatose patients who do not suffer from diabetes—as, for instance, in saturnine encephalopathies, etc.—diacetic acid is often found in the urine. Von Jaksch has proposed to give the name of "coma diaceticum" to these cases of coma. Nevertheless, neither acetone nor diacetic acid and oxybutyric acid have very prominent poisonous properties. Kussmaul gave animals 6 grams of acetone per day without effect. Buhl, Tappeiner, and Frerichs came to similar results. Albertoni found the lethal dose of acetone for dogs to be about 6 to 8 grams per kilogram of the dog's weight.

Geelmuyden draws the conclusion from many experiments on rabbits that, even when small (10 to 20 mg.) subcutaneous injections of acetone are given, the acetone is excreted with the urine; in larger doses more acetone is excreted; but only a portion of the injected quantity reappears; another portion of it is excreted with the expired air; but still a portion is left which does not reappear and must therefore have been disintegrated in the body of the animal. After the injections albuminuria takes place. An adult rabbit can bear an injection of 2 grams of acetone, but is killed by the injection of 6 grams. In starving animals the experiments gave the same results; a portion of the injected acetone reappeared in the urine and the expired air, while still another portion was disintegrated in the body. Geelmuyden draws from these experi-

ments the conclusion that the acetonuria observed in starving individuals is not caused by a diminution of the power to disintegrate acetone already formed in the body, but to an increase of the amount of acetone formed in the body.

Modern authors generally admit that acetone is a product of the metabolism of proteids. Hönigmann and von Noorden are of the opinion that acetone is only formed by diminution of the organized albumin of the body, and never by the metabolism of the proteids ingested with the food, be the quantity ever so large. Hönigmann supported this theory principally by experiments made on himself, which proved that when he lived exclusively on large quantities of proteids—that is, when nutrition was insufficient—acetone and diacetic acid were found. The acetonuria was not augmented when more albumin was ingested, but disappeared when he took plenty of carbohydrates in addition to the proteids. Von Engel, on the contrary, is of the opinion that in all cases when great quantities of albumin are decomposed in the body the quantity of acetone excreted with the urine will increase considerably,—equally if the albumin is ingested with the food or taken from the stock of the body.

Weintraub and Hirschfeld are decided opponents of this theory. Weintraub argues that—in a case of severe diabetes where complete equilibrium of the metabolism, and especially of the metabolism of nitrogen, was maintained for a long time, so that no albumin contained in the tissues was consumed—acetone, diacetic acid, and beta-oxybutyric acid were constantly excreted with the urine; the diet was free from carbohydrates; when, also, the quantity of proteids was somewhat reduced the sugar disappeared after twenty-four hours; the weight of the body was maintained, but acetone and diacetic acid were still excreted (Magnus-Levy).

Carbonate of soda augmented the quantity of acetone excreted, without diminishing the quantity of oxybutyric acids. When, in periods of twenty-four hours, no food at all was taken, acetonuria was greatly increased. Ingestion of carbohydrates diminished the acetonuria, even in persons suffering from diabetes; levulose, milk, and sugar have the same property; glycerin, also, as observed by Hirschfeld. The addition of fat to the food has no power to arrest the acetonuria.

Hirschfeld found that when he put two individuals on light diet, consisting only of proteids and fat, diminution of albumin of the body, as well as acetonuria, was produced. When carbohydrates were added to the food the acetonuria diminished, and that to a much greater degree than the diminution of albumin. Ingestions of fat had absolutely no influence in diminishing acetonuria, although it diminished the loss of nitrogen. Acetonuria is more marked when the albuminous food is scarce than when it is given in great quantities. The ingestion of carbohydrates has an extraordinarily rapid effect on the production of acetonuria, the quantity of acetone being considerable within two hours.

Experiments in persons who were almost starving have proved that a moderate quantity of carbohydrates was sufficient to bring about marked diminution of acetonuria in spite of

the considerable loss of albumin and fat which still took place.

Geelmuyden, from his experiments on rabbits and dogs already mentioned, reached the conclusion that acetone is formed in the tissues, not in the kidneys; that the kidneys give passage to the acetone, even when their blood contains a very small quantity of it, and that pathological acetonuria is not caused by a defect of disintegration of acetone in the body, but by a disorder of the general metabolism leading to the formation of an anomalous large quantity of acetone. Geelmuyden has further conducted a series of experiments in healthy individuals (medical students) put on different scales of diet, which were strictly controlled. As all observers did, Geelmuyden found that when a person was put on exclusive flesh diet acetonuria appeared, and at the same time the body lost albumin as well as fat; when large quantities of proteids were ingested, acetonuria was less considerable than when less albumin was given. Complete starvation, an exclusive fat diet, and a diet of proteids, with the addition of a great quantity of fat, cause a very considerable amount of acetone to be excreted. As exclusive diet of fat and complete starvation give rise to the excretion of the largest quantity of acetone, it seems that acetone is formed by disintegration of fat, and that in this respect there is no difference between the fat of the food and that of the tissues. Carbohydrates have a great power to check the excretions of acetone; when individuals were put on a diet without carbohydrates and secreted urine containing a great quantity of acetone, the acetonuria disappeared in a few hours when carbohydrates were given. From 150 to 200 grams of carbohydrates per day are required to check an already existing alimentary acetonuria.

In the opinion of Geelmuyden, acetonuria occurs when carbohydrates are not ingested in sufficient amount, and acetone is formed by the disintegration of fat, either of that of the tissues or of that contained in the food. Schwarz and Waldvogel saw also an increase of acetonuria following the fat introduction per os.

PRELIMINARY TESTS FOR ACETONE.—With an alkaline solution of sodium nitrocyanide (of a slightly red hue) acetone gives a ruby-red color, changing, after some time, to yellow, and, after acidifying with acetic acid and boiling, to greenish violet.

The cyanide of soda test, after Legal or le Nobel (see below), may be employed as preliminary test; but, to make the presence of acetone positive, it is necessary to separate it from the urine by distillation. As the boiling point of acetone is low (56.3° C.), this may be done at a low temperature, and the use of a water bath is recommended.

Legal's Test.—To 10 c.c. of urine a small crystal of nitrocyanide of soda or some drops of a freshly made solution of this reagent are added; the fluid is rendered strongly alkaline by a 30 per cent. solution of caustic soda or potash. When acetone is present a beautiful red color will appear, which will change only after some time to yellow; the red color produced in the same manner by creatinin becomes yellow sooner. Legal adds that, when acetone is present and the urine, shortly after the

addition of the solution of soda, is neutralized with acetic acid, the urine assumes a purple-red color, and, when diluted with water, a crimson hue. When the acetic acid is floated on the urine a crimson ring will appear at the point of contact, and, when much acetone is present, the color of the ring will be purplish red.

> Legal's test is rendered simpler and more reliable by substituting ammonia for the sodium hydrate. This avoids the disturbing creatin reaction. The urine to be tested is treated with glacial acetic acid and then with a few drops of a freshly prepared solution of sodium nitroprussid; a few cubic centimeters of ammonia are then cautiously poured on top of the mixture. In case of the presence of acetone, a bright-violet ring appears at the point of contact. The violet ring grows brighter and brighter without spreading wider, irrespective of the quantities used in the test-tube or conical glass. The reaction was most distinct in the writer's tests when 15 c.c. of urine and from 0.5 to 1 c.c. of acetic acid were used. Acetone, 0.025 per cent., is readily detected by this test. Alcohol and aldehyde do not give the reaction. Lange (Münch. med. Woch., Bd. liii, Nu. 36, 1906).

Le Nobel's Test. — Le Nobel and Fehr hold that Legal's test is only reliable when much acetone is present, and that, when there is only a small quantity of it in the urine, the test may be fallacious, since other substances contained in the urine can produce a red color with the nitrocyanide of soda. The most characteristic point of the test is, according to Fehr, the appearance of the violet hue, which causes the red color to become crimson or purple, and not pure red.

Le Nobel proposes to substitute a solution of ammonia for the solution of soda, when the test is, in other respect, made according to the indications of Legal; the fluid containing acetone is not immediately colored, but after some time, when the liquid is shaken with air or some drops of a strong acid added (the alkaline reaction being maintained), the fluid takes a rose-red color, increasing gradually and changing after some time to violet wine red. By heating the fluid the color disappears, but returns on cooling down; when boiled with acids it changes into greenish violet. Le Nobel's test is more delicate than Legal's, and will reveal 0.00025 gram of acetone.

Lange thinks the contact reaction gives a more distinct picture than the mass reaction, and modified le Nobel's test in that direction: 15 cm. of urine are mixed in a reagent glass with 0.5 to 1 c.c. of acetic acid and a few drops of solution of sodium nitroprusside. On floating a small amount of ammonia upon this mixture an intense violet ring develops at the point of contact.

> When 15 c.c. of urine are mixed in a reagent glass with from 0.5 to 1 c.c. of acetic acid, and a few drops of a freshly prepared solution of sodium nitroprusside are added, upon floating a small amount of ammonia upon this mixture an intense violet ring develops at the point of contact if acetone is present. The test will detect acetone in a $\frac{1}{400}$ per cent. solution. This is merely a convenient modification of the le Nobel reaction, and has the advantage over Legal's test of not reacting to creatinin. The writer thinks the contact reaction gives a more distinct picture than the mass reaction. It has an advantage over the iodoform reaction in that alcohol and aldehyde do not give it. It is, however, not nearly so sensitive as the latter. Lange (Münch. med. Woch., Bd. liii, S. 1764, 1906).

Jackson Taylor also modified le Nobel's test. He adds strong ammonia to a fresh-prepared solution of sodium nitroprusside and urine. The ammonia solution remains on the top. There appears—if acetone be present—a well-marked and absolutely characteristic ring of magenta (or petunia) within one to three minutes, and gradually spreads upward, pervading the whole of the ammonia solution if acetone is present in considerable amount.

Fehr's Test. — Fehr also employs the test after the method of Legal, but proposes, when the color of the urine after the addition of solution of soda is passing from dark red to yellow, to float some drops of acetic acid on the urine. When the test-tube is slightly rotated so that only a small quantity of the acid mingles with the urine, a beautiful violet color will appear when acetone is present, the intensity of the color being proportionate to the quantity of acetone contained in the urine.

Chautard's Test. — Romine recommends, as a reliable test for acetone in the urine, a solution of fuchsin (1 : 2000) into which a current of sulphurous acid gas has beeen passed. This rapidly decolorizes the liquid and causes it to assume a clear yellow tint, which is permanent and unaffected by an excess of acid. A few drops of such a solution, added to a urine containing acetone, produce a deep violet color. The test is delicate enough to allow the detection of 1 part of acetone in 1000 of urine.

DEFINITE TESTS FOR ACETONE.—When no very great quantity of acetone is found in the urine it is absolutely necessary to distill the urine and to test the distillate with the different reagents. The distillation of 200 to 300 c.c. of urine (always fresh, since acetone can disappear when the urine has to stand hours in a warm place) is made in a water bath, and a temperature of 56° to 58° C. employed. No acid need be added to the urine before distillation, as the acetone becomes distilled very well without acid and the acid might disintegrate other substances present and thus cause the formation of acetone. There is no reason why special care should be taken lest a small amount of ammonia be distilled with the acetone. The distillation is only continued until a sufficient quantity of fluid for the different tests to be employed has passed over into the recipient. The distillation is then subjected to the following tests :—

Lieben's Iodoform Test.—To a few c.c. of the distillate a few drops of a solution of potassium and some drops of a solution of iodine and iodide of potassium are added, the solution of potassium being added in excess. When acetone is present, a thick, yellow precipitate of iodoform will immediately form. This test will reveal 0.01 mg. By heating, the iodoform evaporates and accumulates on the sides of the test-tube in the form of small yellow plaques, consisting of the characteristic crystals (hexagonal plaques and stars) of iodoform. The most serious objection to Lieben's test is that many (at least seventeen) other substances, and especially alcohol, may give the same result.

The most satisfactory test for acetone in the urine is Lieben's. It is performed by adding a few drops of Lugol's solu-

tion to the first 10 c.c. obtained by distilling 400 c.c. of fresh urine, then adding sodium hydroxide solution until the brown color disappears. In the presence of acetone a milky precipitate of iodoform is produced, and may be recognized by its violet coloration with caustic soda and thymol, or by its yellow hexagonal crystals under the microscope. Ronsse (Annales de Gyn. et d'Obstét., Mar., 1900).

Gunning's Test.—Gunning modified Lieben's test by using a solution of ammonia and tincture of iodine. Le Nobel prefers to use a solution of ammonia and iodine dissolved in iodide of ammonium; this certainly is the best way to make the iodoform test, as no alcohol is added with the reagents. According to le Nobel, 0.001 mg. of acetone can be detected by this test, but von Jaksch could only detect acetone by it when present in a quantity of 0.1 mg. Errors caused by the presence of alcohol and aldehyde are avoided by this test.

Reynold's Test. — Freshly precipitated oxide of mercury is dissolved by acetone in the presence of alkali. Le Nobel prefers to make the test by precipitating a solution of perchloride of mercury with an alcoholic solution of caustic potash, added until the mixture gives a strong alkaline reaction; then the fluid containing acetone is added and the whole well shaken in a test-tube. The fluid is then filtered and care taken that the filtrate be perfectly limpid. The combination of acetone and oxide of mercury in the filtrate can be detected by chlorate of stannum or by floating some drops of the filtrate on a solution of sulphide of ammonium: where the two liquids touch each other a black ring will appear. By means of this test 0.01 mg. of acetone is revealed, but aldehyde is also able to dissolve a rather considerable quantity of mercuric oxide.

The Nitrocyanide Test.—This test is made with the distillate quite in the same manner as with the urine, either after the method of Legal or after le Nobel's modification of it. This test is less delicate, and the phenols, which possibly might have passed over into the distillate, are apt to give the same color as the acetone; the test, therefore, gives no proof of the presence of the latter substance.

Penzoldt's Indigo Test. — Baeyer and Drewsen found that acetone forms indigo blue with orthonitrobenzaldehyde. Penzoldt has employed this reagent by dissolving crystals of orthonitrobenzaldehyde in boiling water; on cooling down the aldehyde forms a white, milky cloud; the fluid which is to be tested is now added and the mixture rendered alkaline with a solution of sodium hydrate. When acetone is present a yellow color will appear, which changes to green and, after ten minutes, to indigo; it also forms an indigo-blue precipitate. Very small quantities of acetone may be detected by shaking the mixture with a few drops of chloroform. When left quiet for some time the chloroform takes a blue color and sinks to the bottom of the test-tube.

According to Penzoldt, acetone is revealed by this test in a solution of 1 to 2000. According to von Jaksch, the smallest quantity of acetone revealed by it is 1.6 mg. Aldehyde acetophenone and other substances form indigo in the same way as acetone, but the color is not so marked.

Malerba's Test. — Malerba found that a ½ per cent. solution of paramidomethylaniline with acetone gives a

reddish color, changing into violet and blue-red.

Riegler describes the following test: 15 cm. of urine are acidulated with 5 to 10 drops of concentrated sulphuric acid. When 2 to 3 c.c. of an aqueous solution of iodic acid are added, an intense pink color will appear, which is not taken up by chloroform. The test is said to be specific and active where Legal's test fails.

Frommer renders the urine strongly alkaline with potassium hydrate and adds several drops of a 10 per cent. solution of salicylic aldehyde, and heats to 70° C. A purple ring appears if the reaction is positive.

Miscellaneous Tests.—With bisulphite of soda, acetone, as well as the aldehydes, combines to a crystallic compound in thin flakes resembling those of cholesterin, even by microscopic examination (Limpricht).

Acetone in an alkaline solution combines with iodine to form iodoform.

Freshly precipitated oxide of mercury is dissolved by acetone. Indigo is formed when acetone is combined with orthonitrobenzaldehyde in an alkaline solution. (Baeyer and Drewsen.)

From what has just been stated it will become apparent that not one of the tests is specific for acetone alone. To be quite sure that acetone is contained in the distillate, it is necessary to try successively by all the tests, and only when all tests give positive result is the presence of acetone proved.

A. E. Taylor is of the opinion that only the tests described by Stock and Denigés are really good and reliable and should replace the tests with Lugol's solution, mercuric oxide and sodium nitroprusside.

> The only two really good tests for acetone in the urine are that of Stock, described in 1899, and that of Denigés, described in 1898. These are certain in their results and easy of execution, and should replace the fallacious tests with Lugol's solution, mercuric oxide and sodium nitroprusside. The two tests agree; the writer has never had the Stock test present without the Denigés test being also positive. The Stock test is less sensitive than the other, but this is considered an advantage for practical purposes. The author has often found acetone present by these tests without obtaining the reaction for diacetic acid, for which he also gives the method; but he has never found diacetic acid present without acetone. A. E. Taylor (Jour. Amer. Med. Assoc., Mar. 17, 1909).

The quantitative estimation of the acetone bodies is often most important as an indicator of the degree of derangement of metabolism and acidosis that may be present.

Von Jaksch has tried to employ the nitrocyanide test for a quantitative estimation of the acetone, and the iodoform test has been recommended by Messinger and Huppert for the same purpose. The quantity of iodine used to form iodoform with the acetone is measured (titrated), and the quantity of the acetone present in the solution calculated by it also; but, although Engel and Devoto are of the opinion that it is possible to make pretty accurate estimations in this way, methods for quantitative estimation of the actone are not to be relied upon, as it is impossible to avoid errors caused by the presence of substances which are influenced by the tests in the same way as the acetone.

Diacetic acid ($C_4H_6O_3$=CH_3—CO—CH_2—COOH) may be revealed in the urine by the aid of a solution of perchloride of iron (Gerhardt's test),

which, with diacetic acid, produces a dark wine-red color. The test is made by adding a solution of perchloride of iron as long as a precipitate of phosphates of iron is formed. The mixture is then filtered and some drops of perchloride are added to the filtrate. When diacetic acid is present, the filtrate takes a deep-red color, which vanishes in twenty-four hours, and more rapidly after addition of strong acids. Von Jaksch has, by a colorimetric method based on this test, tried to make an approximate estimation of the quantity of diacetic acid contained in the urine, but newly passed urine can alone be used for the search of diacetic acid, as this acid, after some time—twenty-four to forty-eight hours—will disappear from the urine. Diacetic acid can be isolated from the urine by adding a few drops of sulphuric acid and shaking the mixture with ether. When diacetic acid is present, it is dissolved in the ether and can be detected by the perchloride of iron test.

Beta-oxybutyric acid ($C_4H_8O_3$) is also found sometimes in the urine of fever patients, as well as in diabetes, with acetone and diacetic acid. This may also be the case in the dyspepsia of alcoholism and in carcinoma of the stomach, scarlatina, measles and scorbutus. When beta-oxybutyric acid is cautiously oxidated, acetone is found.

For general practice the exact quantitative determination of the acetone bodies is rather complicated. To overcome this difficulty, Stuart Hart (1908) devised a procedure based on the delicacy of the well-known test-tube reactions in urine. The urine is first tested for Gerhardt's reaction. If positive, we know the acetone bodies to be present in excess of 0.2 Gm. per liter. If the reaction is very strong, the test solution is diluted with distilled water until the color approximates that of the standard ferric chloride solution, and this dilution, when compared in one of the author's tables, gives the amount in Gm. per liter. If Gerhardt's reaction is negative, Arnold's, Legal's and Lieben's tests are tried in the order named. A positive Arnold reaction indicates Ca 0.1 Gm. per liter; positive Legal reaction Ca 0.03 Gm. per liter. If only Lieben's test is positive, the amount of acetone is within the normal limits.

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ACETOZONE, a germicide and deodorant (accepted by the A. M. A. Council) formerly known as *benzozone,* is a mixture of acetylbenzoyl peroxide and an inert absorbent powder. It was introduced by Freer and Novy, of the University of Michigan. Its properties resemble those of hydrogen peroxide, though, according to its discoverers, it is over one hundred times more active as a germicide.

Acetozone, in its original form, occurs as white shining crystals, but is marketed in the form of a powder. The latter should be kept perfectly dry, but it should not be exposed to heat, which decomposes and volatilizes it. It is also rapidly decomposed by organic substances and should not be administered after a meal.

Modes of Administration.—Acetozone is usually employed in the following manner: "Add the powder to warm water in the proportion of 15 grains to the quart; shake vigorously for five minutes, and allow to stand for about two hours. Decant off the liquid as required. If the patient objects to the taste, a little extract of orange or lemon, or orange or lemon juice, ginger ale, carbonated water, or fruit syrup may be added to each dose as taken." It may also be given in capsules, but followed at once by a copious draught of water.

It is soluble in water to the extent of 1:1000 to 10,000; in its crystalline form in oils to the extent of about 3 per cent. and slightly soluble in alcohol, ether, and chloroform, but all these solvents gradually decompose it. This does not apply to neutral petroleum oils, however, and an *"acetozone inhalant"* is available which contains 1 part of acetozone, ½ part of chloretone, and 98.5 parts of refined liquid petroleum. It may be given in an *ointment,* using solid or liquid petrolatum as excipient, beginning with ½ per cent. strength. An aqueous solution may be used as *spray* and as a *deodorizer* and *antiseptic* for stools, sputum, etc.

Therapeutics.—Acetozone is used for its marked oxidizing and germicidal action mainly for the treatment of diseased mucous membranes. It has been credited with a favorable action in **typhoid fever,** the main effect being decrease of the fetor of the stools, subsidence of the tympanites and diarrhea, and prevention of hyperpyrexia. Good results have been obtained in **Asiatic cholera.** In ophthalmology, a solution of 1 grain to 2 ounces of water, instilling 1 drop or 2 every hour, has been found useful in **corneal infections.** In laryngology, **tonsillitis** and **atrophic rhinitis** have seemed to be beneficially influenced. This applies also to **infected wounds, gonorrhea,** and **chancroid.** It has been found an excellent deodorant in **gangrene** and malignant **small-pox.** S.

ACETPARAMIDOSALOL.

See SALOPHEN.

ACETPHENETIDIN.—

(*acetphenetidinum;* para-acetphenetidin), commonly known under the proprietary name of *phenacetin,* is a coal-tar product, obtained by treating paraphenetidin with glacial acetic acid. It is an acetyl derivative [C_6H_4. OC_2H_5. NH CH_3CO] of para-amidophenol.

PROPERTIES.—Acetphenetidin occurs in the form of a white, odorless, and practically tasteless powder, composed of small, needle-like or scaly crystals.

DOSE.—Five to 10 grains (0.32 to 0.65 gram) in adults; 1 to 5 grains (0.065 to 0.32 gram), according to age, in children. The *maximum* amount to be given in twenty-four hours, according to Pouchet, is 30 to 45 grains (2.0 to 3.0 grams), which should be distributed during the day in several doses, each not exceeding 7½ grains (0.5 gram). The tendency is toward a marked decrease of this amount.

> Out of 297 observers using acetphenetidin, 10, or 33 per cent., employed less than 2 grains as a minimum dose for adults; 90, or 30.3 per cent., employed 2.5 grains or less as a minimum dose; 188, or 63.3 per cent., employed from 3 to 5 grains as a minimum dose; 89, or 29.9 per cent., used doses exceeding 5 grains, while 208, or 70 per cent., never exceeded a dose of 5 grains.
>
> An examination of a number of prescriptions for adults on file in various pharmacies in Washington, D. C., showed that the average dose of acetphenetidin prescribed was 1.92 grains. Kebler, Morgan, and Rupp (U. S. Dept. of Agricul., Bureau of Chemistry, Bull. No. 126, July 3, 1909).

MODES OF ADMINISTRATION.—Acetphenetidin is almost insoluble in cold water (1 grain in 2 ounces), more freely soluble in boiling water (1 grain in 1 dram), and readily so in alcohol (1 grain in 12 minims); it will also dissolve in glycerin and lactic acid.

Being almost tasteless, it is easily taken in powder form; it can also be given in capsules, cachets, or tablets. When combined with other remedies in liquid preparations it is best kept in solution by dilute alcohol. Thus a mixture of acetphenetidin, sodium bromide, and caffeine in the adjuvant elixir is frequently prescribed for the relief of headache. A good formula is the following:—

℞ *Acetphenetidini* ..... gr. xv (1.0 Gm.).
Caffeinæ citratæ ..... gr. viij (0.5 Gm.).
Sodii bromidi ..... ʒj (4.0 Gm.).
Elixir adjuvantis ... ʒj (30.0 c.c.).

M. Sig.: Two teaspoonfuls, repeated if necessary. Shake well.

Where nausea and vomiting accompany headache, oral administration being, therefore, unsuitable, acetphenetidin may be administered by the rectum in 1 or 2 drams of water (Brunton).

Acetphenetidin is sometimes used locally in powder form or in an ointment or alcoholic preparation.

INCOMPATIBILITIES.—Acetphenetidin is incompatible with iodine, nitric acid, and oxidizing agents generally; also with chloral hydrate, phenol, and salicylic acid.

CONTRAINDICATIONS.—These are the same as those of acetanilide (*q.v.*), though the dangers from its use are less marked than with the latter drug. It is advisable not to employ it in cases of heart disease, pulmonary tuberculosis, grave anemia, or in persons markedly enfeebled from any other cause.

PHYSIOLOGICAL ACTION.—As Antipyretic.—Acetphenetidin is the safest and most frequently employed of antipyretic remedies. In common with acetanilid, it has little or no influence on the temperature of normal individuals in therapeutic doses, but causes a fall in febrile cases. According to Crombie and Hirschfelder, the greatest reduction is not produced until three or four hours after administration. The average decline may be put down as 3.6° F. (2° C.; Manquat). The reduction may last six to eight hours, and is free of unpleasant effects, excepting a mild sweat (Pesce). Cerna and Carter found that acetphenetidin produced a very slight fall of temperature during the first and second hours after ingestion, and that the effect reaches its height in the third hour. They believe that the fall of temperature results chiefly from a decrease in heat production, together with a slight increase in the heat dissipation, less marked than in the case of antipyrin. Probably the delayed action of the drug depends on its insolubility. It should be mentioned, however, that certain authors describe its effect as being more prompt, and comparable with that of acetanilide.

With regard to the manner in which the antipyretic effect is produced, the prevailing belief is that it depresses the heat-regulating centers.

[Viewed from my standpoint, the action of acetphenetidin differs only from that of acetanilide (*q.v.*) in that it excites less violently the sympathetic center, owing to its greater insolubility. As the sympathetic center governs the caliber of the arterioles (see "Internal Secretions," vol. ii, 1907), its excitation causes constriction of these small vessels and a reduction of the volume of arterial blood admitted into the tissues. This entails a reduction of temperature in the latter, (1) owing to the lowered metabolic activity which the diminution of arterial blood in the superficial tissues entails, and (2) because the adrenals and the thyroid, which jointly, as I have shown, supply the substances which in the blood sustain oxidation and metabolism, are themselves rendered less active by the diminished blood-supply. It is therefore, by *exciting* the sympathetic center, that acetphenetidin produces its effects. This reduces heat production by inhibiting both the functional activity of the adrenals and thyroid and tissue metabolism. C. E. DE M. S.]

As Analgesic.—Acetphenetidin is considered to exert a sedative effect upon the nervous system. Its anodyne influence is more marked than that of acetanilide or antipyrin. It is believed to depress the nerve-centers, in common with the other antipyretics, but it has probably also some action on the sensory nerves, since it frequently relieves

neuralgic pain without giving evidence of any central depressant action by the production of drowsiness or mental apathy.

Injected into animals, large doses of acetphenetidin are required before its effects on the nervous system appear. Using doses of 0.5 to 1 Gm. per kilo of body weight in rabbits, Mahnert observed merely a muscular weakness, lasting a few hours, which he ascribed to a depressing action on the spinal cord. With doses of 3 Gm. per kilo he obtained a short period of spinal excitation, followed by one of complete motor and sensory paralysis, with loss of reflexes and early death. In frogs the preliminary spinal excitation may be such as to produce convulsions. In mammals convulsions produced by the antipyretics may be of cerebral, spinal, or, possibly, asphyxial origin (Cushny). H. C. Wood, Jr., and H. B. Wood watched the effects of acetphenetidin on frogs when absorbed through the skin from a saturated solution. Like Mahnert, they noted a sluggishness of movement and loss of muscular power, proceeding steadily to complete paralysis, with final cessation of the heart beats. In addition, they found that the motor nerves and the muscles, though soaked in saturated acetphenetidin solution, continued responsive to electric stimulation throughout the period of action of the drug, and even after death, and concluded, therefore, that the loss of reflexes and paralysis observed had been of spinal origin. They ascertained that doses of 0.5 Gm. per kilo, injected into the jugular vein of a dog, caused death from paralysis of respiration.

Local applications of acetphenetidin have some analgesic effect.

[The reduction of pain is also due to the constriction of the arterioles the drug produces. Less blood being admitted into the painful area, the sensory nerve terminals are no longer hyperemic, and they cease to transmit painful impressions.

The same process explains all the experimental phenomena: the muscular sluggishness, the paralysis, the cardiac arrest, etc., since diminution of the blood supplied to a tissue reduces in proportion its functional activity. The convulsions are due to the accumulation of toxic wastes (as in epilepsy, tetanus, etc.), owing to imperfect catabolism, the latter process being under the dependence of the (now inhibited) adrenals and thyroid. C. E. DE M. S.]

On the Circulation.—Conflicting views have been advanced by different observers concerning the effects of the drug on the blood-pressure. Cerna and Carter found that, in moderate doses, it caused a rise of the arterial pressure by directly stimulating the heart's action, and also, probably, the vasomotor system, while in large doses it decreased the pressure, chiefly by its influence on the heart. They also state that acetphenetidin tends to increase the pulse rate, mainly by cardiac stimulation, and possibly, also, by influencing the cardio-accelerator apparatus, while later, especially with large doses, it decreases it primarily by stimulating the cardio-inhibitory centers, and later by depressing the heart. Ott and H. C. Wood, Jr., on the contrary, assert from their experiments that acetphenetidin does not influence the blood-pressure. Mahnert considers the drug to be antagonistic to strychnine in its physiological action, large doses producing paralysis of the cardiac and respiratory centers. In the early stage of its action, however, it is believed to stimulate these centers for a time.

[The influence on blood-pressure noticed by some observers is due to the fact that the constriction of the arterioles produced by the drug causes these vessels to impede the flow of blood into the capillaries, and to

cause the blood to accumulate behind the obstruction, thus causing a back pressure in the large vessels. As soon as the dose is large enough to inhibit the heart's action by reducing the blood supplied to its walls, this organ is unable to keep up the pressure—in keeping with Cerna and Carter's view. Large doses thus fail to produce a rise of the blood-pressure. C. E. DE M. S.]

On the Blood.—Alterations in the blood are much more rarely caused by acetphenetidin in moderate doses than by acetanilide. The formation of methemoglobin has, however, been observed in a few cases. According to Cushny, this untoward result is due to the action of para-amidophenol, into which the drug is gradually decomposed in the organism. Cerna and Carter were unable to produce methemoglobinemia in their experiments on animals.

Acetphenetidin is said to have a slightly stimulating influence on the sweat-glands, which is not possessed by the other antipyretics.

[When the dose is very large or the sympathetic center is abnormally sensitive, the arterioles are sufficiently contracted to reduce the supply of blood to the tissues below their normal needs. The blood is not only rendered venous abnormally soon under these conditions by the intense reducing power of the tissues, but the hemoglobin molecule itself is broken down, methemoglobin being formed. C. E. DE M. S.]

Elimination.—Acetphenetidin is believed to be eliminated chiefly in an altered condition, losing its acetyl radicle in transit through the organism, and appearing in the urine as glycuronates of phenetidin (Cushny). The gastric and pancreatic juices being without influence on the drug *in vitro,* F. Müller believes that the decomposition must occur after it has been absorbed. According to Gueorguievsky, the elimination by the urine begins in twenty minutes and proceeds rapidly. Perchloride of iron added to this urine causes a Burgundy red color to appear. Acetphenetidin may also be eliminated in part by the skin, since Hirschmann not infrequently found large numbers of crystals precisely similar to those of the drug on the skin of persons to whom it had been administered.

UNTOWARD EFFECTS AND POISONING.—H. C. Wood states that no symptoms are produced by the therapeutic dose of this drug. Even large doses of it have been given so often without markedly unpleasant results that, in contrast with acetanilide and antipyrin, it has frequently been described as non-toxic. Massive doses, however, and even moderate doses in certain susceptible individuals, have been known to cause untoward effects similar to those of the other coal-tar antipyretics. The most commonly observed of these have been profuse sweating, somnolence, lassitude, sometimes accompanied by nausea, vertigo, or chilliness. In more severe cases there have occurred cyanosis, beginning and most marked in the face, lips, and finger-tips, then becoming general; prostration, vomiting, palpitation, dyspnea, anxious expression, followed by collapse, which occasionally is fatal. The blood may be darkened by the formation of methemoglobin. The urine has been found to contain blood (Krönig). In a case reported by Hollopeter three doses, of 7 grains each, of phenacetin sufficed to produce in a woman severe precordial pains, great dyspnea, general lividity, somewhat dilated pupils, and collapse, with unconsciousness; recovery took place after a week. Cutaneous eruptions, usually urticarial, are sometimes caused, though less frequently than by antipyrin. As with acetanilide, the onset of the symptoms is frequently sudden and unexpected, the patient hav-

ing previously borne repeated doses without harmful effect.

[All the morbid effects of large doses of acetphenetidin are the result of the excessive constriction of the arterioles it causes. The sweating is due to ischemic relaxation of the spiral muscles of the sweat-glands; the vertigo and somnolence to cerebral ischemia; lassitude to the same condition of the muscles; the chilliness and cyanosis to cutaneous ischemia and the too rapid conversion of arterial into venous blood, etc. C. E. DE M. S.]

Case of a woman suffering from ovaritis and acute dysmenorrhea, who took 5 to 8 cachets containing each 10 grains (0.65 Gm.) of acetphenetidin in twenty-four hours. She suddenly complained of palpitation of the heart; her face was brilliantly scarlet with the exception of the bridge of the nose and the upper lip, which were markedly pallid; the pulse was extremely rapid, and she also suffered from headache, dyspnea, and diaphoresis. There was no urinary or gastric disturbance. John Harold (Practitioner, Dec., 1894).

Two cases in which acetphenetidin caused dyspnea and orthopnea. In the first case 15 grains (1 Gm.) every four hours were taken for some time with impunity, but after thirty-six hours the patient repeated the dose in two hours, the result being marked shortness of breath and extreme restlessness. In the second case 20 grains (1.3 Gm.) were administered every two hours until 2 drams (8 Gm.) had been taken, when dyspnea resulted and continued for an hour. J. L. Lackie (Medical Press and Circular, Aug. 28, 1895).

Fatal case of acetphenetidin poisoning in a boy 17 years old suffering from chronic middle-ear disease, who had taken 4 powders, of 15 grains each, within three weeks. Sepsis having set in, a fifth dose, taken one evening, brought on vomiting, followed by giddiness, great weakness, and cyanosis of the face and lips. The temperature was 102.2° F., the pupils of medium size, the pulse weak, and the patient complained of headache, vomiting, and diarrhea. The conjunctivæ were slightly yellowish, and a general icteric appearance followed, combined with blueness of the lips, ears, hands, and feet. The blood contained red cells in various stages of dissolution and of different sizes and shapes. Particles of hemoglobin were set free in the plasma. There was marked leucocytosis. The urine, obtained by catheter, was thick, dark reddish brown in color, later containing masses of almost pure blood. Death occurred in two days, with universal methemoglobinemia. G. Krönig (Berl. klin. Woch., Nov. 18, 1895).

Eight grains of acetphenetidin taken every three hours for headache. After the third dose, the patient became very ill, and his face became pale. Shivering, cold perspiration, and dyspnea followed. Wheals developed on the backs of the hands and right shoulder, and the face became swollen and of a mahogany color. Recovery followed. W. A. Betts (Brit. Med. Jour., Jan. 18, 1896).

Petechial eruption on the legs, followed in a week by ulceration, reported as the result of taking acetphenetidin. Upon stopping the drug the ulcers quickly healed, but after another dose of 22½ grains they reappeared. M. Hirschfeld (Deut. med. Woch., Nu. 31, 1905).

The exhibition of 15 grains of acetphenetidin every two hours for twenty-four hours resulted in marked feebleness, followed by symptoms of collapse, with faintness, dizziness, dyspnea, cyanosis of the limbs, combined with a general yellowish-gray color, pain over the heart, nausea, and a rapid, weak pulse. On the following day a macular eruption made its appearance. Recovery took place in five days. J. Meurice (Ann. de la Soc. de Méd. de Gand., No. 85, 1905).

Fatal case of poisoning in a woman of 50 suffering from muscular rheumatism, who had taken on the same day 2 powders each containing 15 grains of acetphenetidin and 3 grains of caffeine sodiobenzoate. Marked pallor appeared, followed by profuse sweating, nausea, vomiting of a cerebral type, and

restlessness. An injection of camphor and a small dose of morphine were given. On the next day the condition became worse, notwithstanding camphor injections every two hours, ammonia, and an injection of normal saline. In the afternoon the patient became unconscious. The pulse was 120; respirations, 30. Progressive cyanosis of the face and limbs ended in death from vasomotor paralysis the same evening. The urine was of a porter-brown color, gave the reactions for methemoglobin, and showed evidence of parenchymatous nephritis in the presence of albumin with hyaline and granular casts. The blood examined after death showed leucocytosis and marked pallor of certain of the erythrocytes. The autopsy revealed fatty and parenchymatous degeneration of the heart, marked hyperemia and edema of the viscera, general arteriosclerosis, and acute nephritis.

The writer believes that alcohol taken with or before the administration of coal-tar antipyretics favors the occurrence of symptoms of poisoning, and that alcohol is, therefore, contraindicated in all cases of collapse due to these drugs. The subjects most intolerant of the coal-tar antipyretics are those that normally perspire freely. K. E. Russow (St. Petersburger med. Woch., Feb. 8, 1908).

[The remark of Russow that alcohol tends to aggravate acetphenetidin poisoning is sustained by my views. While the latter tends to interfere with oxidation by diminishing the volume of blood admitted into the tissues, alcohol becomes oxidized at the expense of the blood, thus increasing the toxicity of the acetphenetidin. C. E. DE M. S.]

A girl of 16½ years, in good general health, but having a headache and feeling that she had taken cold, took 2 headache tablets and went to bed. About an hour and a half later her lips and face began to grow blue, and a physician was sent for. Responding at once, he found the girl with pronounced cardiac weakness and edema of the lungs. Before any remedy could be administered she died. The tablets she had taken, labeled "Danbury's headache tablets," were subsequently found on examination to contain acetphenetidin. G. L. Tobey (Mo. Bull., State Board of Health of Mass., Jan., 1908).

Of 70 cases reported by 41 observers in the literature from 1887 to 1907, 3, or 4.2 per cent., terminated fatally. Sixty-three of the 70 cases were reported during the years 1887-90, *i.e.,* in the period just following the advent of acetphenetidin as a medicinal agent, when the drug was used freely in asthenic as well as sthenic affections. The most prominent ill effect was general systemic depression, which was present in 38.5 per cent. of the cases. In 17.1 per cent., it amounted to actual collapse. Cyanosis was reported in 34.3 per cent. of the cases, skin affections of various kinds in 30 per cent., dyspnea in 14.3 per cent., and disturbances of the renal function in 10 per cent. Kebler, Morgan, and Rupp (U. S. Dept. of Agricul., Bureau of Chemistry, Bull. No. 126, July 3, 1909).

Of 306 physicians questioned on the subject of acetphenetidin poisoning, 66, or 21.5 per cent., stated that they had observed instances of poisoning (as compared with 76 per cent. of 288 physicians having seen instances of acetanilide poisoning). These 66 observers reported 95 cases of poisoning by acetphenetidin, including 7 deaths, *i.e.,* 7.3 per cent. The character of the fatal cases and the doses used were as follows:—

Pneumonia, 70 grains daily for two days; died suddenly.

Influenza, 5 grains every three hours; not over 6 doses.

Bronchitis (1 year), 2 grains every three hours; 5 doses; died twelve hours after last dose.

Typhoid, 2½ grains every two hours until 1 scruple was taken.

Headache, 10 grains.

Headache (cerebral tumor), 15 grains in twelve hours.

Woman, aged 76, two 3-grain doses two hours apart.

Kebler, Morgan, and Rupp (U. S. Dept. of Agricul., Bureau of Chemistry, Bull. No. 126, July 3, 1909).

Treatment of Acute Poisoning.—No special reference to this subject having been found in the literature, we can only recall the plan of treatment used for poisoning by the other coal-tar derivatives, the toxic effects of which are identical. Stimulants to the circulation and respiration, such as **strychnine, atropine, aromatic spirits of ammonia, ether** hypodermically, and **digitalis; saline solution** by enteroclysis or hypodermoclysis, etc. The application of **heat** to the body should never be neglected in cases of collapse. **Artificial respiration** is always valuable, and inhalations of **oxygen** may be resorted to as an ultimate measure.

[Of the foregoing the only drugs that I do not regard as harmful in cases of acetphenetidin poisoning are, in the order given: the aromatic spirits of ammonia and the salt solution, which jointly, by increasing the alkalinity and osmotic properties and fluidity of the blood, tend to reduce its toxic action on the sympathetic center and relax the constricted arterioles; the application of heat to the surface and inhalations of oxygen. Strychnine, atropine, ether, and digitalis all tend to aggravate the trouble by increasing, if anything, the constriction of the arterioles.

The agents indicated—only from my viewpoint—are those which cause dilatation of the arterioles by depressing the sympathetic center: amyl nitrite by inhalation, and nitroglycerin to sustain the effect, or sweet spirits of niter, the latter in full doses. C. E. DE M. S.]

CHRONIC POISONING.—While not as frequent as chronic acetanilide poisoning, chronic acetphenetidin poisoning is nonetheless fairly common. The symptoms show a great similarity to those produced by the habitual use of acetanilide, consisting chiefly of nervous and digestive disturbances, a cyanotic coloration of the skin, anemia, and weakened heart action.

Case of a woman, previously "a healthy, buxom country girl," who had been addicted to the acetphenetidin habit for about seven months, ingesting from 15 to 20 grains daily. The habit was found out by her husband when her supply of the drug gave out and the local pharmacist also ran out of a supply temporarily. Violent convulsive and hysterical seizures appeared, and continued until acetphenetidin had been obtained for her. The pulse rose to 170 and became feeble; respiration, 30, spasmodic; pupils widely dilated; pallor and cold perspiration. The patient had over a dozen convulsions and vomited freely. Examination subsequent to the attack showed some anemia, poor complexion, weak circulation, pulse 124, sleep restless and troubled, digestion impaired, occasional vertigo. J. S. Davis (Amer. Med. and Surg. Bull., July, 1894).

Case of acute dysentery reported in which the exhibition of approximately 3000 grains of acetphenetidin in 5-grain doses within sixty days for fever was followed by marked depression and rapid dilatation of the heart resulting in death. The fatal ending could fairly be ascribed to chronic poisoning by the drug. A. T. White (Jour. of Tropical Med., June, 1903).

From collective reports of cases it would appear that toxic manifestations are somewhat less likely to develop when acetphenetidin is taken habitually than when acetanilide is the drug used.

In the replies of 400 physicians to a set of questions sent out by the Bureau of Chemistry of the U. S. Department of Agriculture, 112 instances of the acetanilide habit were reported, 7 of the antipyrin habit, and 17 of the acetphenetidin habit. The number of cases in which ill effects were observed from the use of acetanilide was 85, from antipyrin 2, and from acetphenetidin 7. The chief symptoms observed from the habitual use of these drugs were: Nervous depression, 44 cases; cyanosis, 27; cardiac depression, 18, anemia, 15; dyspnea on exertion, 8; insomnia, 4; constipation, 3; edema, 2; increased

headache, 2; icterus, 1; muscular twitchings, 1; loss of sexual power, 1. In 5 of the cases of acetphenetidin habit protracted ill effects were noted, as compared with 32 instances in case of acetanilide and 2 instances in case of antipyrin. The chronic symptoms oftenest noted were anemia, general debility, nervousness, and weak and irregular heart action. Kebler, Morgan, and Rupp (U. S. Dept of Agricul., Bureau of Chemistry, Bull. No. 126, July 3, 1909).

Treatment of Chronic Poisoning.—The measures required upon withdrawal of the drug will generally comprise the use of **stimulants, saline laxatives,** and **codeine,**—the latter used with caution in amounts just sufficient to mitigate pain and favor sleep (*v.* Treatment of Chronic Acetanilide Poisoning).

THERAPEUTICS.—As Antipyretic.—Acetphenetidin is generally considered the safest of the coal-tar antipyretics. Its effect in reducing temperature is marked; as previously stated, its action begins in about thirty minutes and reaches its maximum in three to four hours. According to Heusner, 1 Gm. (15 grains) of this drug is the equal in antithermic power of 0.5 Gm. (7½ grains) of acetanilide, and 2 Gm. (30 grains) of antipyrin. The relative infrequency with which it causes cyanosis, depression, and other unpleasant or dangerous effects recommends its general use as an antipyretic in preference to the older coal-tar remedies if used at all. The employment of antipyretics other than hydrotherapy and other external measures is decidedly on the wane, however, in the hands of competent clinicians.

Exception to this is probably only to be made where prompt reduction of fever is required, as in cases of hyperpyrexia; here acetanilide, whether used in conjunction with hydrotherapeutic measures or not, may prove more effective than acetphenetidin. It is believed, however, that the effect of the latter drug is more lasting than that of acetanilide; the greater tendency of which to depress the circulatory and respiratory organs should also be remembered. As stated above, however, the use of antipyretics in the various forms of fever is now deemed inadvisable by most authorities. Moreover, these agents, by causing the temperature records to lose their characteristic features, may impair their value for diagnostic and prognostic purposes. The alleged prejudicial influence, on the other hand, that chemical antipyretics have been said to exert on the substances of the blood-serum that antagonize disease has been shown not to exist, at least in the case of the agglutinating bodies of typhoid serum (Sollmann). When delirium is present in fever, the mild narcotic action exerted by the coal-tar antipyretics, and in particular by acetphenetidin, may prove advantageous.

[The cardinal feature still overlooked is that fever is the external expression of the process through which the body defends itself against infection. When hyperthermia is present (over 105.5° F.), however, there is good ground for the belief that the immunizing process is so active that the blood-cells and tissues may also be digested by the defensive blood constituents (hemolysis and autolysis) along with the bacteria and their toxins. It is then, especially in such diseases as pleurisy, endocarditis, acute rheumatism, which, from my viewpoint, are mainly due to excessive proteolytic activity of the blood, that acetphenetidin can find a useful application in fever.

It should be remembered that the surface temperature is often the expression of too slow elimination of heat from the superficial tissues, where the febrile process is very active, and that cool sponging by taking up

this accumulated heat lowers the temperature promptly to the great relief of the patient. C. E. DE M. S.]

As an Analgesic.—Phenacetin is chiefly of value for the relief of pain, especially of pain of the neuralgic type. In pains due to gross inflammations or deep-seated distress, the result of organic disease of viscera, morphine is far more effective than phenacetin. But in pains due to nervous disorders, especially **neuralgia** and **neuritis**, and in various forms of **headache**, acetphenetidin has come to be considered almost as a specific. In **hemicrania**, in **headache due to eye-strain or insufficiency** of certain of the extraocular muscles, in **intercostal neuralgia**, **sciatica**, **gastralgia**, and in the pains of **tabes dorsalis**, acetphenetidin frequently affords considerable relief.

The manner in which this drug, in common with other coal-tar antipyretics, acts in relieving headache has not yet been definitely ascertained. According to Brunton, headache is associated with and caused by what he terms a "colic" of the arteries of the head, the peripheral vessels being contracted and the central vessels dilated; the drug would presumably give relief by overcoming this abnormal condition of the cephalic arteries. E. Weber has recently demonstrated experimentally in dogs whose brain had been exposed that coal-tar drugs cause constriction of the vessels on the surface of the cerebrum.

It is well known, moreover, that caffeine, an undoubted vasoconstrictor, when combined with the coal-tar drugs, greatly assists their analgesic action in headaches. Hence it would seem as if the relief given in these cases were due, in some way, to a modification in the caliber of the vessels.

[Weber's experiments (Arch. f. Physiol., p. 348, 1909) confirmed the conception of action of coal-tar antipyretics which I had advanced in 1907 in "Internal Secretions," etc., vol. ii, pp. 1282 to 1299, in which I showed that the reduction of pain was due to constriction of the arterioles and the resulting diminution of arterial blood admitted to the sensory terminals. C. E. DE M. S.]

In **acute rheumatism**, acetphenetidin has been found useful as an analgesic in doses of 3 to 8 grains (0.2 to 0.5 gram), given every four hours. A valuable combination is 4 grains each of acetphenetidin and salol, given three or four times daily. Eldredge counsels the administration of acetphenetidin in powder and salicylic acid in solution, the dose of each being regulated according to the patient's susceptibility and the severity of the attack. In cases with cardiac complications, he claims not to have observed any depressing action on the heart when the drug was given to reduce fever. Hirschfelder noted specially the fact that sometimes a hypnotic action seemed to be produced. In **subacute rheumatism** and in **lumbago** and other **rheumatic muscular pains**, the drug is also frequently effective.

In **gonorrheal rheumatism**, acetphenetidin was found by Eldredge to act well when given with potassium iodide and sodium salicylate.

In **influenza**, acetphenetidin has become a favorite remedy. The pains in the head, back, and limbs are relieved, and the fever reduced. The drug may be given alone in powder form, or combined with other remedies, *e.g.*, quinine. In this disease, essentially an asthenic disorder, it is important that the analgesia be secured with the least possible degree of general depression; hence acetphenetidin should always be given the preference over its more depressing congeners—acetanilide and antipyrin.

In **whooping-cough**, acetphenetidin diminishes the severity and frequency of the paroxysms. In children, 1 or 2 grains (0.06 to 0.013 gram), given three or four times daily, are generally sufficient.

Chorea has also been treated with acetphenetidin. Like the other coal-tar drugs, acetphenetidin exerts a not inconsiderable effect on the motor functions and reflex action, as well as on general sensibility. Hence the fact that it sometimes proves useful in this disorder.

Insomnia, the result of overwork or general nervous excitability, may yield to acetphenetidin. Kiernan reported having seen it bring on sleep in persons suffering from insomnia due to simple exhaustion. In view of the possible serious depressive effects from an overdose, the likelihood of a drug habit being formed, and the fact that much safer and better hypnotics are available, it seems doubtful whether the use of acetphenetidin for this purpose should be encouraged.

The same is probably true of the use of acetphenetidin in the initial stage of **pneumonia**, in which it has been employed to relieve distress, bring on sweating, reduce fever, and favor sleep. If the drug is used at all, it must surely be withdrawn as soon as the patient begins to show pronounced general depression and signs of lowered circulatory activity. In pleurisy acetphenetidin has likewise been used to relieve the pain of the initial stage.

The first stage of **acute coryza** may be shortened by giving a few doses of acetphenetidin, which will not only promote sweating and lower the temperature, but also relieve the unpleasant accompanying sensations. A powder containing 5 grains (0.3 gram) each of acetphenetidin and salol, together with 1 grain (0.06 gram) of citrated caffeine, may be administered every three hours for 3 doses with advantage.

In **diabetes mellitus** acetphenetidin, in common with other coal-tar drugs, has been prescribed, generally with but temporary benefit.

Local Uses.—Acetphenetidin is sometimes used externally for its analgesic and antiseptic properties. Dusted in finely powdered form on the raw surfaces of **ulcerations** of various kinds, it not only relieves pain, but favors the development of healthy granulations, thereby hastening the healing process. Because of its low degree of solubility in water, as compared with antipyrin and acetanilide, the likelihood of the absorption of a toxic amount of acetphenetidin from open surfaces is somewhat less than with the above-mentioned agents. Nevertheless, this danger should always be kept in mind, and the external use of the drug confined to lesions covering a small area only.

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ACETYLENE.—When calcium carbide (CaC_2) is brought in contact with water, acetylene gas is formed. Being capable, when ignited, of furnishing a degree of light far superior to that of ordinary gas, acetylene has in recent years been considerably used as an illuminant. When prepared from pure calcium carbide and purified by liquefaction, it has a pleasant ethereal odor and can be breathed in small quantities without giving rise to ill effects. Impure gas, prepared from coal or impure lime, may contain calcium sulphide and phosphide, and the acetylene prepared from it may then have a very unpleasant odor.

Acetylene Poisoning.—Acetylene may be fatally poisonous when present in propor-

tions as high as 40 per cent. by volume, as shown by Gréhant, Berthelot, and Moissant. A mixture of 20 volumes of acetylene—prepared from calcium carbide, 20.8 volumes of oxygen, and 59.2 volumes of nitrogen—was breathed by a dog for thirty-five minutes without any marked disturbance, and 100 c.c. of the blood were found to contain 10 c.c. of acetylene. With 40 volumes of acetylene, the proportion of oxygen remaining the same, a dog died in less than an hour, owing to failure of the heart's action, and 100 c.c. of blood contained 20 c.c. of acetylene. With 79 volumes of acetylene and 21 volumes of oxygen the poisonous effects were still more strongly marked.

The poisonous action of acetylene itself is feeble when the blood is at the same time supplied from the air with the usual amount of oxygen. In other words, acetylene inhaled in the open air is but slightly harmful. Brociner found that 100 volumes of blood dissolve about 80 volumes of acetylene; the solution shows no characteristic spectrum, and is reduced by ammonium sulphide as readily as ordinary arterial blood. If any compound of acetylene and hemoglobin is formed, it is very unstable, and is not analogous to carboxyhemoglobin.

In a closed room, however, where the oxygen is not kept up to the normal standard, when the accumulation of a foreign gas would prevent the constant renewal of air through window and door interstices or open chimneys, and where the products of respiration would be allowed to accumulate, it would quickly prove mortal by paralyzing the respiratory function. Mosso and Ottolenghi found experimentally that acetylene has considerable toxic power. One pint of the pure gas caused severe symptoms of poisoning in dogs, and even when mixed with air (20 per cent.) it proved fatal after an hour. If the gas was administered rapidly, the animal recovered when placed in the open air, but if given slowly this did not occur, and the animals died.

Thomas Oliver has shown that a mixture of air and acetylene commences to be explosive when it contains 5 per cent. of acetylene, whereas it requires the presence of 8 per cent. of coal gas to make a similar mixture explosable. If a rabbit is placed in a bell-jar into which ordinary air and acetylene are pumped, the animal seems for a long period to experience very little inconvenience. It is not until ordinary atmospheric air is excluded and only acetylene admitted that symptoms gradually and slowly develop. After a more lengthened exposure to acetylene than that which is necessary for coal gas the animal becomes intoxicated, it falls over on its side apparently profoundly asleep, and, while all through the experiment its breathing has been somewhat short and rapid, stupor steals over the animal apparently painlessly. A few inhalations of atmospheric air are sufficient to restore to the animal all its faculties. Should inhalation have been pushed further and the animal have been very deeply asphyxiated, death may ensue, cyanosis, hitherto observed, being rapidly replaced by extreme pallor.

Treatment of Acetylene Poisoning.—That **fresh air** should at once be given the patient need hardly be mentioned. The patient should be removed from the poisoned atmosphere into a well-ventilated room and **artificial respiration** practised. Hypodermic injections of **strychnine** and **digitalis** should be administered while **oxygen** is sent for. This gas should be inhaled as soon as practicable, while artificial respiration is continued with vigor, the patient being simultaneously rubbed. **Rectal injections of warm coffee** are also useful. **Hypodermoclysis,** with **epinephrin** or **adrenalin** 1 : 1000 solution introduced drop by drop into the **saline solution** by pushing the hypodermic needle into the rubber pipe, is indicated in all cases of severe poisoning by the gas.

In all such cases the efforts of the physician should be kept up a long time, the respiration and pulse being unreliable guides as regards the presence in the system of sufficient life to render resuscitation possible. S.

ACIDITY OF THE GASTRIC CONTENTS, TESTS FOR.—While the acidity of normal gastric juice is due mainly to the presence of hydrochloric acid, departures from the normal proportion of this acid in the gastric contents have been

found to accompany with sufficient frequency certain disorders to facilitate the recognition of these disorders. Thus, a proportion of hydrochloric acid of 0.15 to 0.3 per cent. represents the acidity found under normal conditions, *i.e., euchlorhydria,* but an excess of acid, *hyperchlorhydria,* is common in gastric ulcer, gastroptosis, hysteria, tabes, and other disorders. *Hypochlorhydria,* a deficiency of hydrochloric acid, also accompanies various disorders, especially gastric cancer, neurasthenia, anemia, chronic gastritis of long duration, gastric neuroses, and certain diseases of the pancreas, while *achlorhydria,* absence of hydrochloric acid, is found in advanced cases of the same disorders. Again, the fact that hydrochloric acid is necessary to peptic digestion, while acting as a powerful antiseptic to the ingested foodstuffs, further indicates the practical importance of ascertaining accurately the acidity of the gastric contents.

To obtain accurate information, it is necessary to administer a test-meal containing a definite quantity of foodstuffs, and to leave the latter in the stomach a definite time.

Test-meals.—Those described are generally given preference:—

The *Ewald-Boas breakfast* consists of 1 roll weighing about 35 Gm. (9 drams) and a large wineglass of 300 Gm. (10 ounces) of water. This meal should be taken early in the morning on an empty stomach, the bread being eaten slowly and the water sipped while this is done. At the end of one hour, 20 to 60 c.c. (5 to 10 drams) of the meal should be withdrawn from the stomach in the manner indicated below.

The *Leube-Riegel test-meal* consists of beef soup, 400 c.c. (12 ounces); beefsteak finely chopped, 200 Gm. (6 ounces); wheat bread or potato, 50 Gm. (1.6 ounces), and water, 200 Gm. (6 ounces). The gastric contents should be removed at the end of four hours.

The *Salzer method* includes two meals: The first consists of 30 Gm. (1 ounce) of lean roast beef chopped very fine; milk, 250 c.c. (8 ounces); rice, 50 Gm., and 1 soft-boiled egg. The second meal, given four hours later, is an Ewald-Boas breakfast, described above. At the end of five hours after the first meal, that is to say, one hour after the second, the gastric contents is withdrawn.

The Salzer test affords, in addition to the opportunity of ascertaining acidity, that of determining the motility of the gastric muscles; for if particles of meat of the first meal are still present at the end of five hours, the propulsive activity of the stomach wall is deficient.

Withdrawal of Gastric Contents.—This, the next step of the examination, is carried out with the aid of a flexible red rubber tube about a yard in length, the catheter-like end of which is provided, a short distance above the tip, with a fenestra or opening. It is an ordinary stomach tube the upper end of which is funnel-shaped. About 2 feet above this end is a mark which, when the tube is introduced sufficiently far, *i.e.,* when its tip reaches the bottom of the stomach, corresponds with the incisor teeth of an adult.

The patient's clothing being protected with a towel tied round his or her neck, the tube, previously warmed by being placed in a bowl of warm wat r and lubricated with glycerin, is introduced, *i.e.,* passed down the esophagus. This is done readily by pushing the end of the tube gently into the latter, over the epiglottis, while the patient swallows, and as often as he does so. In some cases, especially the first time, the procedure may cause gagging, but this can be avoided by passing the tube on one side of the epiglottis, *i.e.,* in either pyriform sinus. The sensitive surface of the pharynx is thus avoided.

To withdraw the gastric contents several ways are available. The easiest is to depress the external end of the tube as soon as the latter is *in situ,* and request the patient to lean forward and cough a few times or contract his abdominal muscles. An essential point, however, is that the (clean) bowl in which the gastric contents is to be collected must be considerably below the level of the patient's stomach, *i.e.,* between his knees, so as to obtain the benefit of siphonage. The expulsion of the gastric contents is facilitated by pressing on the stomach while the patient is coughing or contracting his abdominal muscles; it is further aided by having him lie down on a lounge, the bowl being placed on the floor. It is not necessary to

empty the stomach, a couple of tablespoonfuls (about 30 c.c.) sufficing for all purposes.

Various pumps, aspirating bulbs, etc., have been invented to deplete the stomach, but they entail the use of parts that are difficult to clean properly, and expose the gastric mucosa to the evil effects of direct suction by the tube. Moreover, complicated instruments tend to increase the timidity of the patient, which, at best, is sometimes difficult to overcome. Briefly, the above-described "simple expression method" is, on the whole, the most satisfactory.

Contraindications to the Use of the Stomach Tube.—In a certain proportion of cases, however, even the use of the simple stomach tube may prove dangerous. They are: cases of advanced cardiac disorder; advanced arteriosclerosis, especially if there is a history of cerebral hemorrhage or "slight stroke"; elderly persons of apoplectic build. In either of these the tube may cause a sudden reflex rise of the blood-pressure and rupture of any diseased vascular tissue. A history of recent hematemesis or of bloody or tarry stools is also a contraindication, since the bleeding may be due to gastric ulcer or cancer, which the extremity of the tube might readily abrade, and thus cause renewal of the hemorrhages. Advanced tuberculosis, marked emphysema, pregnancy, and extreme debility are also recognized as contraindications.

Determination of Free Acids.—The mere presence of any free acid, hydrochloric, lactic, etc., can readily be determined by using paper previously dipped in a solution of *Congo red* and dried. This turns blue in the presence of free acids, but does not identify one acid from another.

To identify hydrochloric acid, the best reagent is probably the *dimethylamidoazobenzol*. It may be used in 0.5 per cent. solution or in absorbent paper allowed to dry before using. The yellow color of either becomes reddish pink in the presence of hydrochloric acid. This test furnishes an inkling as to the degree of acidity due to the latter, for the reddish-pink color becomes much deeper in proportion as the percentage of acid is great.

Tropeolin is another good reagent which can be used in the same manner. Its yellowish-brown alcoholic solution turns red in the presence of both hydrochloric acid and lactic acid; but the former can be differentiated by spreading a few drops of a saturated solution in a porcelain dish, and adding thereto an equal quantity of the gastric fluid. On mixing them and heating them gently, blue and lilac stripes (formed by hydrochloric acid only) appear.

An extremely delicate test, which will detect 1 part of hydrochloric acid in 20,000 parts of water, is *Gunzburg's*, whose reagent consists of:—

℞ *Phloroglucin* ..... 2 Gm. (30 gr.).
Vanillin ..... 1 Gm. (15 gr.).
Absolute alcohol ..... 30 c.c. (1 oz.).

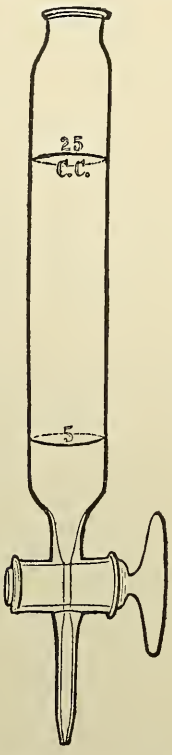
It should be kept in a dark bottle. By adding a few drops of this reagent to the gastric filtrate and allowing the mixture to evaporate to dryness, a beautiful rose-red tinge is obtained if free hydrochloric acid is present.

To Ascertain the Total Acidity.—The easiest method is to add 1 drop of a 1 per cent. solution of *phenolphthalein* to 10 c.c. (2½ drams) of the gastric fluid, after filtering the latter, and neutralizing the mixture by a given quantity of decinormal solution (about 30 grains to the pint—2 Gm. in 500 c.c. of distilled water) of sodium hydroxide. The technique of the procedure is as follows: Place 10 c.c. of the filtered gastric fluid in a beaker, and add thereto 2 drops of phenolphthalein solution. Then add the decinormal sodium hydroxide solution from a *graduated* burette (mixing with a glass rod) until a permanent red or reddish-pink color appears, which means complete neutralization. Now, the number of c.c. (say 4 or 4.5) of sodium hydrate solution necessary to obtain the latter, as shown by the graduated burette, with a naught to the right of this figure (making 40.0 or 45.0 of the above figures), will represent the percentage of total acidity.

A watery solution of Congo red may be used instead of phenolphthalein. As we have seen, free hydrochloric acid in the gastric fluid or chyme changes the red color to blue. If, now, decinormal sodium hydrate solution (*vide supra*) is slowly added to the mixture until the Congo red

is restored, the number of cubic centimeters of the sodium hydrate solution required to obtain this result will represent the amount of free hydrochloric acid.

Lactic acid, which suggests the presence of cancer or dilatation, being contained in all bakery products, in meats as sarcolactic acid, sour milk, sauerkraut, and sour gherkins, a special meal is necessary to eliminate from the test the acid due to



Strauss's separating funnel for lactic acid test.

foods. A bowl of soup prepared with Knorr's oatmeal, rendered palatable by adding common salt, suffices for this purpose. *Uffelmann's reagent* may then be used. It is composed as follows:—

℞ *Solution of carbolic acid* (4 per cent.) ..... 10 c.c.
Distilled water ..... 20 c.c.
Official neutral ferric chloride solution ..... 1 drop.

This should be prepared fresh for each test. Its amethyst-blue color will be turned to canary yellow when added to the gastric filtrate.

A quantitative estimation of lactic acid may be obtained by *Strauss's method.* "A separating funnel (shown in the annexed cut) with marks at 5 c.c. and 25 c.c. is filled to the first mark with gastric juice and then to the second with ether. After thoroughly shaking, the fluid is allowed to flow out to the first mark (5 c.c.), then filled with water to the second mark (25 c.c.). Two drops of a 10 per cent. solution of iron chloride are then added. A beautiful green color appears in the presence of amounts exceeding 0.5 per mille." (Lenhartz-Brooks.)

Butyric acid and other fatty acids, on boiling the gastric filtrate, emit a characteristic odor. They also turn yellowish brown in the presence of *Uffelmann's solution,* just described. Another test is to shake the gastric product (unfiltered) with acid-free ether, and then allow the latter to evaporate. On adding *calcium chloride* to a watery solution of the residue, the butyric acid forms oil droplets with the characteristic odor of the acid.

Acetic acid also emits a characteristic odor, that of vinegar. A small quantity of gastric filtrate, say 10 c.c., is treated with ether as above. The residue being dissolved in a little water and neutralized with a solution of sodium carbonate, a couple of drops of a very dilute solution of ferric chloride are added. The filtrate then becomes dark red if acetic acid is present. Or a few drops of sulphuric acid and alcohol may be added to the same neutralized residue; on heating, the latter then gives off the characteristic vinegar-like odor of acetic acid. S.

ACIDOSIS. See AUTOINTOXICATION.

ACNE.—DEFINITION.—Acne is characterized by the presence, usually on the face, of small elevations or nodosities varying in size from a pinhead to a pea. These elevations, or pimples, are also present on the back, shoulders, and chest in many cases.

SYMPTOMS.—The elevations are conical or hemispherical, and, as a

rule, in the earliest stage of the lesion somewhat painful, especially upon pressure. In most of the lesions there is a distinct tendency to suppurative change. In the center of the lesion a whitish-yellow spot forms where the pus raises the epidermis. In from three to ten days, or even longer, the lesion breaks and a small amount of pus is discharged. At other times the pus dries to a thin crust, or occasionally the contents, especially in sluggish lesions, are absorbed. A red elevation is left which gradually flattens out, leaving a brownish stain, which eventually disappears. The surrounding skin is frequently oily and shiny. Small, sluggish, abscess-like lesions, and tumors as large as a pea or a small nut, formed by retention cysts of sebaceous glands, are sometimes seen; they may gradually work to the surface or may persist for months and finally disappear or form hard spherical indurations by retraction and inspissation of their contents. Scarring, usually consisting of small, white, cicatricial depressions, is to be seen as a consequence in some cases. In the majority of cases, however, permanent marks are not left. The regions most affected in acne are the face, shoulders, and anterior and posterior aspects of the shoulders. Occasional cases are observed in which the back, extending as far down as the sacrum, is the chief seat of the disease. In rare instances (acne cachecticorum, acne scrofulosorum, and acne medicamentosa) the eruption may be more or less general.

VARIETIES.—There are several varieties of lesion observed in acne, one kind of which is apt to predominate, and this has given rise to the so-called varieties of the disease.

Acne vulgaris, or *acne simplex,* is, by far, the most common clinical type. The lesions are usually of a mixed character, consisting of blackheads, pinhead- to pea-sized papules, papulo-pustules, and pustules. Each lesion may in its beginning have a small, red areola. There is also slight pain upon pressure. The lesions are rapid in evolution, running a course in several days to a week. As in all types, they are discrete and isolated.

The term *"acne papulosa"* is given to a not uncommon type in which the lesions are usually small and show but little disposition to reach the pustular stage, disappearing by absorption or by desiccation and exfoliation.

Acne punctata might be termed minute papular, the lesions being, for the most, pinhead in size, with a central comedo, or blackhead.

Acne pustulosa is another type in which the lesions go rapidly into the pustular stage, the eruption appearing, for the most part, to be made up, almost entirely, of pustules. In size they vary from a large pinhead to a large-sized pea.

Acne indurata, or *"tuberculosa,"* is a form of the eruption in which the lesions tend to be closely crowded here and there and in such places, and also with single lesions, the underlying base becomes hard, inflamed, and indurated, being also somewhat deep-seated.

In *acne phlegmonosa* the inflammatory and suppurative process begins deep down in the sebaceous gland, forming veritable small dermic and intradermic abscesses, usually with but slight tendency to break through the surface.

Acne cachecticorum characterizes an acneic eruption, more or less general,

occurring in weak, cachectic individuals; the lesions are livid, indolent, violet-red papulopustules of moderate and large size and of slow evolution, leaving, as a rule, small cicatrices. Acne scrofulosorum is really a variety of the last named,—acne cachecticorum,—occurring in those of distinctly strumous or tuberculous temperament.

Acne artificialis seu medicamentosa is a form of acneic eruption produced by the ingestion of certain drugs, as the iodides and bromides, and also by the external applications of certain remedies, such as tar, the paraffin oils, etc.

"Acne atrophica" is a name given to those cases of acneic eruption which tend to leave depressed scars. This probably occurs most frequently in those cases in which the lesions are sluggishly papular or papulopustular, the lesions disappearing by absorption or crusting and leaving behind small, punched-out cicatrices.

Acne hypertrophica is really the opposite of the last-named variety, and occurs in about the same kind of cases, small, whitish, connective-tissue, pinpoint or small-pea sized projecting hypertrophies marking the sites of the lesions. It is rare.

ETIOLOGY.—Acne begins usually near puberty, when the pilar system is more actively developing, and the functions of the sebaceous glands likewise; and is more frequent among patients with digestive troubles, constipation, dilatation of the stomach, menstrual irregularities, the strumous diathesis, possibly the arthritic diathesis, and disturbances of the nervous system.

Acne at about the time of puberty may be of intestinal origin, and in 94.9 per cent. of a series of 33 cases of acne occurring at this age the writer found clear evidence of abnormal putrefactive changes in the intestine, as shown by the presence of an excess of indican, phenolcresol, etc., in the urine; this intestinal putrefaction may be due to the peristaltic inertia common at about the time of puberty. Although further investigations are needed to demonstrate the causal connection between acne and excessive intestinal putrefaction, the writer tried the effect in cases of acne of drugs which have an antifermentative action and which aid peristalsis, and with this object has administered a combination of 1 gram of sulphur precipitate and 0.25 gram of menthol, given two or three times a day over a period of several months. In the 33 cases of acne mentioned, which included cases of acne simplex, acne pustulosa, and acne indurata, treatment on these lines was very successful, substantial improvement being seen in all the cases and recovery in many. In 1 case the medicine gave rise to diarrhea with colic-like pains, but in the others there were no unpleasant side-effects. The first result of the treatment was that the stools became pultaceous and the output of phenol sank to 0.01, or at the highest to 0.07, as opposed to an average output of 0.101 gram, which had been previously observed. With this fall in the output of phenol improvement began, and often in the first three or four weeks the acne papules were observed to more quickly disappear; during the next four in eight weeks, in all but 1 obstinate case, new papules appeared with much less frequency, and in 9 cases, after three months' treatment, no new papules formed. Some of the cases have now been as long as eighteen months without relapse, and may be considered to have completely recovered. During the internal treatment, local treatment, although it was not altogether discontinued, was reduced to a minimum. Josef Kapp (Therapeutische Monats., March, 1907).

It has been also alleged without, however, substantial foundation that

lesions of the genitourinary organs and venereal excesses may provoke the disease. Lesions may be due to mechanical irritation caused by the product of secretion remaining in the excretory canal or gland itself. Some drugs, as already stated,—such as the bromides and iodides,—are occasionally responsible for the eruption or an increase in an already existing eruption. Certain drugs applied externally may also provoke acneic lesions, such as tar and tar products, juniper oil, and the like. Workers in paraffin and paraffin products will not infrequently be found affected with papules and pustules, especially those of a furuncular or abscess type. The direct local exciting factor is thought, by many, to be a micro-organism, Gilchrist's observations pointing to a specific bacillus.

> Up to 1899 no observer had succeeded in obtaining the acne bacilli pure from lesions of acne vulgaris or comedo, and there was practically no proof that these bacilli were the cause of acne vulgaris. Definite bacilli (*Bacillus acnes*), however, were found present in all smears taken from 240 typical acne lesions from 86 patients. Pure cultures were obtained from 62 lesions (chiefly acne nodules) from 29 patients. It is present as a short, thick bacillus in smears, but in culture often becomes much longer and thicker, and in old cultures assumes distinct branching forms. It is now definitely proven that this micro-organism is the primary cause of acne vulgaris. T. C. Gilchrist (Jour. of Cutan. Med., Mar., 1903).

PATHOLOGY.—In most cases the process begins by a perifolliculitis, which later on gives rise to a purulent folliculitis. It would thus seem that in some cases the sebaceous glands play but a small part in the affection. In most cases, however, when comedones are present, the sebaceous gland itself is the starting point of the inflammatory process. (Brocq.)

Even when the focus of irritation is in the follicle, it is frequently limited to the sebaceous or sebaceous pilary canal. (E. Besnier, A. Doyon.)

The papillæ surrounding the comedone and the superficial layers of the corium are filled with blood-vessels full to repletion, and of exudation cells which are found in dilated vacuoles. (Kaposi.)

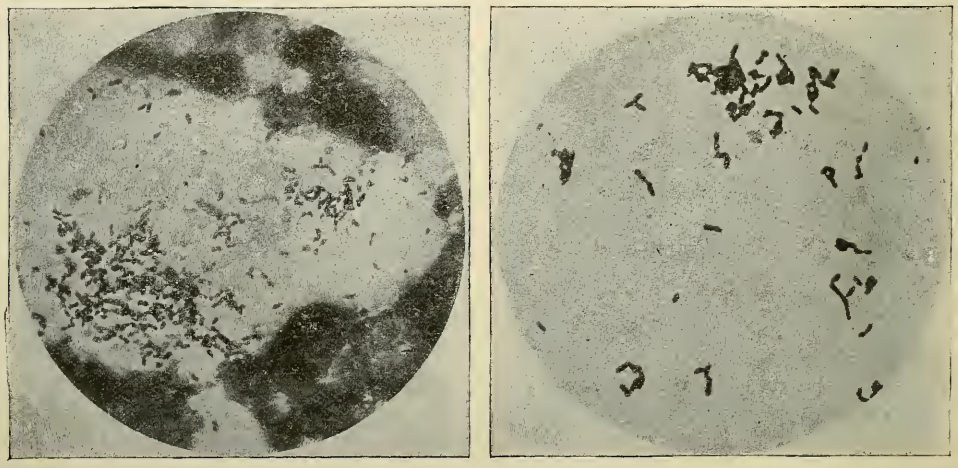
If the process is very intense, the sebaceous gland may be entirely destroyed by the local inflammatory action, while the pilar bulba persists. (Kaposi.)

The acneic process may be divided into two parts: 1. Closure of the sebaceous follicle and formation of comedo. 2. Suppuration, which only occurs in those follicles where the staphylococci aureus et albus have penetrated before the comedo formed. (Unna.)

> The writers have succeeded in growing the *Bacillus acnes* under anaërobic conditions. It stains by Gram's method and often shows an irregular or beaded appearance. It is moderately wide and of variable length, especially in cultures, where it frequently shows branching forms. It forms no spores. Abstracting oxygen, by Wright's method, it grows on all the common media, best on glucose agar, either in suspension or slant. In bouillon it forms a white flocculent sediment. It was most easily grown from the lesions by smearing the pus on the surface of glucose-agar slants. On this medium, in the absence of oxygen, it produces fair-sized colonies in three to five days. It forms raised, grayish-white, opaque colonies, considerably smaller than those of the staphylococcus albus, which are purer white. On acid agar, as noted by Flemming, it grows in the presence of oxygen, but much more slowly. The bacillus is, therefore, essentially an an-

aërobe, but will grow in the presence of oxygen when planted in masses, by reason of the anaërobic conditions which are thereby created within the masses. They regard this bacillus as identical with the *Bacillus acnes* of Gilchrist and other observers from its similarity in morphology and cultural characteristics. From the ease with which it could be obtained from their cases when grown anaërobically, they think it can probably be cultivated from all cases of acne. Hartwell and Streeter (Boston Med. and Surg. Jour., Dec. 16, 1909).

TREATMENT.—In this connection acne may be divided into (1) an *irritable* or inflammatory variety, in which the skin is fine and thin and easily irritated by stimulating applications, and where general treatment is important on account of the close union between the acneic eruption and various constitutional disturbances. Local treatment should, at first at least, be of a mild character. (2) An *indolent* variety, where the integument is thick, rough, and oily, with enlarged and obstructed gland orifices, and where the most energetic local applications are well borne; here the local treatment is important. Probably most of the cases met with occupy a middle ground between these two extreme varieties.



Bacillus acnes (*Hartwell and Streeter*)
Boston Medical and Surgical Journal, Dec, 16, 1909.

DIAGNOSIS.—Acne is to be differentiated from the papular, papulopustular, and pustular syphiloderms, and also from variola.

Syphilis.—In the syphilitic eruption the distribution is more or less general, and more acute in its outbreak, darker hued, and occurring occasionally with special groupings and the presence of other symptoms of the disease.

Variola.—In small-pox the premonitory constitutional symptoms, the sudden outbreak, the uniformity of the lesions, and many other symptoms of differential character will serve to differentiate.

General Treatment. — Prophylactic measures, such as the avoidance of external irritants, drugs and food liable to cause acne, such as coffee, tea, alcohol, pure wine, pork, veal, game too far gone, preserved fish, shellfish, fats, and cheeses.

Any disorder of digestion must be

counteracted in order to avoid the congestion of the face following meals.

If the tongue is much coated and shows prominent papillæ, the following is recommended:—

℞ *Sodium bicarb.* ..... 10 grs.
Ext. cascara sagr. liq...... 10-20 mins.
Tinct. nux vomica ..... 7-10 mins.
Peppermint water..to make 1 fl. oz.—M.

Constipation should be counteracted by gentle **aperients.** Any condition capable of maintaining the sympathetic system in a state of tension—such as genitourinary troubles or affections of the nasal fossæ—should be eradicated if possible.

If the patient is lymphatic and has a good digestion, **codliver oil** is of value.

Anemia or chlorosis calls for the use of **chalybeates** with **arsenic.** Iron often does harm unless its constipating effect is counteracted by using aperients. When the patient is arthritic, **alkalies,** especially alkaline waters, are indicated.

No really specific treatment is known against acne, but the following have been recommended:—

Sulphur alone: powder or tablets, or with equal parts of honey.

Ichthyol (Unna):—

℞ *Ichthyol* ..... 1-2 drs.
Dist. water ..... 5 drs.

M. Sig.: Fifteen to 50 drops in water, to be taken morning and evening.

Arsenic bromide in weak doses, $\frac{1}{60}$ grain, in acne pustulosa. (Piffard.)

Mercurial preparations, such as **corrosive sublimate** or **calomel,** either alone or with **jalap** or **colocynth extract,** have been found useful.

The writer strongly recommends the old **mistura acidi ferri,** or **Startin's solution,** in plethoric girls with costiveness, coated tongue and local hyperemia. The mixture is as follows:—

℞ *Magnesii sulph.* ..... ℥j (30.00).
Ferri sulph. ..... gr. x (0.65).
Sodii chloridi ..... ℥ss (1.95).
Acidi sulph. dil. .... ℥ij (8.00).
Infusi gent......q. s. ad ℥iv (120.00).

As to the local treatment: 1. Wash the face well at night with cold or tepid water and good soap; tincture of green soap is desirable. Open with a sharp lance all pustules, scrape off the acne tops, use the comedo expressor, dry the face and whiten with the white lotion. 2. In the morning flick off the white powder with a soft towel. It is not then necessary to wash the face. Use the **ointment of sulphur** in the morning if the skin feels dry and harsh in spots or places, or apply the lotion lightly if about the house. 3. On going out use the powder as a cosmetic, and at night wash the face and begin the treatment again. Brayton (Jour. Indiana State Med. Assoc., Apr., 1908).

Summary of treatment: Prohibit cakes, pies, pastries, salt meats, fish, and eating between meals. If anemic, give nourishing foods. **Ferri citratis,** ℥ij; **magnesii sulphatis,** ℥v; **strychninæ,** gr. j; syr. **zingiberis,** ℥j; aquæ, ℥iv. In obese, constipated, and sluggish individuals: **Potassium acetate,** ℥v; fl. ext. of **carcara sagrada,** ℥ij; fl. ext. of **rumex,** ℥iij; 1 dram in water half-hour before meals. **Outdoor exercise.** Where comedones or pustules: **Green soap,** ℥j; **resorcin,** ℥j; **salicylic acid,** gr. v; **rose-water ointment,** ℥ij; to be applied at night and washed off in morning, until fair desquamation obtained. Lotio alba (**potassium sulphide and zinc sulphate**) applied at night after using hot or cold water; friction with towel. Cocks (Med. Record, Dec. 3, 1910).

Local Treatment. — Constitutional treatment will rarely succeed alone, while in a large proportion a local treatment by itself will be found efficacious.

The majority of cases can be greatly benefited in a short time, and very many of them cured promptly. The indications for treatment are as follows: The condition of the skin should

be improved so that it will no longer be a suitable culture ground for the bacillus. The follicles of the skin should be emptied of the colonies of bacilli. The skin should be constantly kept aseptic, so that any bacilli that escape on it will be killed, and no new infection of the skin will be possible. The first indication is met by attention on the patient's general health by means of baths, diet, exercise, attention to hygiene, and, lastly, drugs. The follicles are emptied by the use of the curette, the acne lancet, and the comedo expressor. The best local application is **sulphur,** preferably in the form of the old lotio alba, the formula for which is: **Zinc sulphate** and **potassium sulpheret,** of each, ʒi-ij; **rose water,** q. s. ad ℥iv. This is to be shaken up before using. **Resorcin** is also useful, as well as **sulphur soap.** The use of the **Roentgen ray** should be limited to intractable cases, and requires great caution to prevent doing harm. G. T. Jackson (Med. Rec., Mar. 18, 1905).

Hot-water and alcoholic lotions sometimes act promptly. In mild cases these are applied at night with very hot water, either pure or combined with **cologne water** or **camphorated alcohol.** The water is gradually reduced until pure camphorated alcohol or cologne water is used. **Boric acid** or **borax** may be added to the lotions: 1 part to 50.

Night and morning the skin should be bathed in very **hot water** (to reduce the congestion), to which **creolin,** or a few drops of the following solution, should be added:—

℞ *Corrosive sublimate* .... 7½ grs.
Tinct. of benzoin ..... 75 grs.
Emulsion bitter almonds. 3675 grs.
M.

E. Lacour (Nord méd., Aug. 15, 1900).

Many of the less severe forms can be cured by prolonged **bathing in hot water.** The water should be soft, and the applications to the face should be made with a soft bathing sponge. The sponge, loaded with water as hot as can be borne, should be applied to the face. The bathing should last about five minutes, and should be done each night and morning; at the same time moderate pressure is applied to the sponge. After the sponging the face should be dried on a soft towel without rubbing, and **bay rum** should be applied freely. The face should not be touched by the hands until the time for repeating the process. W. L. Hunt (Jour. of Med. and Sci., Sept., 1904).

Have patient vigorously scrub his face, every night before retiring, with **green soap** and **hot water.** After rinsing with cold water and drying the face, the following paste is to be applied: **Betanaphthol,** 5 parts; **precipitated sulphur,** 25 parts; **green soap** and **lanolin,** of each, 35 parts. Spread this over the involved area and allow it to remain fifteen minutes to one hour, after which it is wiped off. Length of application depends on the reaction produced; if left on too long, the skin reddens, or, after greatly prolonged contact, the epidermis desquamates. This paste acts probably by causing an inflammation of the skin, which extends along the dilated follicles, thus inhibiting the secretion and producing shrinkage of the dilated sebaceous glands. When the condition is improved, continue the applications at longer intervals to prevent recurrence; also scrub face every second or third night. Burke (Penna. Med. Jour., March, 1911).

Instead of camphorated alcohol there have been used with success:—

Alcohol, 96°, saturated with **boric acid,** and **alcohol** with **salicylic acid,** 1 to 30. The latter is strong and must be used with care.

Mercurial preparations have been variously extolled, but in late years have gradually given way to other more valuable remedies.

Mercurial lotions are efficacious in some cases, employed as follows:—

℞ *Corr. subl.* ..... 1 part.
Alcohol, 90° ..... 100 parts.
Dist. water or *rose water* ... 150 parts.

At first this solution is weakened with one-half its quantity of water; afterward, if no irritation has resulted, the water is gradually reduced until the solution is employed pure.

Other **mercurial preparations**, in ointment form, such as the biniodide, the iodochloride, white precipitate, and mercurial plaster, viz.:—

The **ammoniated mercurial ointment**, 5 grains, or 30 grains to 1 ounce, is highly recommended by Stopford Taylor.

Gordon Campbell recommends the following procedure:—

The face is to be washed with water as hot as can be borne and some bland unirritating soap, and then, after carefully drying the skin, the following lotion is applied once a day:—

℞ *Hydrargyri chloridi corrosivi.* 12 grs.
Spiritus vini rectif...... 6 oz.—M.

Effect for first few days will be to render condition worse; but, after this, the lotion prevents perforation of the pustules.

> External drug treatment in both acne vulgaris and acne rosacea is usually disappointing. **Sulphur** is the best external preparation. Mechanical treatment, such as the use of **hot water, soap, massage,** and the **dermal curette,** is exceedingly valuable. The **opsonic method** in acne vulgaris is promising. **Roentgen treatment** of both diseases is the most valuable. In its certainty of cure and frequency of relapse it almost approaches a specific. The technique of using the X-ray, say, in acne, is of paramount importance. If the ray is properly applied there should be few, if any, failures and no undesirable effects. Cole (Jour. Indiana State Med. Assoc., Mar., 1909).

Formaldehyde, largely diluted, has recently been tried with success.

Sulphur preparations are by far the most valuable in the external treatment of the disease; especially useful when much seborrhea exists. In a few patients sulphur preparations cannot be used, owing to the irritation caused. Sulphur may be employed in the following ways:—

Sulphur soap: with hot water, the suds being allowed to dry on to the face.

Sulphur baths.

Sulphur lotions: hot water with 10 to 60 drops for every one-half glassful of liquid **potassium polysulphide.**

An effective method of using sulphur is the following:—

After washing with hot water and soap, the following mixture is applied with a camel's hair brush:—

℞ *Precipitated sulphur,*
Potassium bicarbonate,
Glycerin,
Laurel water,
Alcohol (60°) .....of each 2 drs.—M.

The coating is left on during nighttime and washed off in the morning with an **emulsion of almond oil,** and the skin is covered with **oxide of zinc** or **bismuth subnitrate ointment** powdered over with fine starch.

When the skin becomes irritated, the sulphur paste should be discontinued and the **zinc ointment** applied alone until the irritation has disappeared.

The following are useful:—

℞ *Sulphate of zinc,*
Sulphuret of potassium..of each 1-4 drs.
Water ..... 4 oz.

℞ *Precip. sulphur,*
Ether .....of each 4 drs.
Alcohol .....to make 4 fl. oz.

℞ *Precip. sulphur* ..... 2 drs.
Gum tragacanth,
Camphor .....of each 20 grs.
Lime water ..... 2 fl. oz.
Water .....to make 4 fl. oz.

Both these lotions are often made more valuable by the addition of 2 to 5 per cent. of **resorcin.**

Sulphur ointments are usually made in the proportion of 1 in 10, with benzoated lard, simple cerate, vaselin, vaselin and lanolin, lanolin and sweet almond oil or olive oil, or castor oil and cacao butter.

To the sulphur may be added **oxide of zinc** in equal parts; **borax,** 1 to 20; **salicylic acid,** 1 to 50; **naphthol,** 1 to 10 or 1 to 20; **resorcin** or **camphor,** 1 to 20 or 1 to 40. They may be perfumed with essence of rose, bergamot, or balsam of Peru if desired.

Sulphur soaps are sometimes more convenient.

The following may be used:—

Soap and precipitated sulphur, equal parts.

Soap, precipitated sulphur, and lard, equal parts.

Naphthol may be cautiously added to the first of the series.

Among other local treatments recommended are the application to the pustules of **carbolic acid, salicylic acid,** or **resorcin.** An ointment of **ichthyol,** 1 to 4 or 1 to 8, is also useful.

> **Ichthyol** is very beneficial both in acne vulgaris and acne rosacea. The best results are obtained when external and internal treatments are combined. In some cases of acne rosacea in which the skin is too thin and irritable to bear even weak solutions, the internal administration of ichthyol alone, with steaming, will be beneficial. Five grains of ichthyol may be given thrice daily, after food, increasing the amount to 10 grains. Every night and morning the face is steamed for fifteen minutes, and is then washed with ichthyol soap. The lather is allowed to dry on the face, after which it is gently washed off with water. After each washing ichthyol salve, if it can be borne (often combined with ammoniated mercury), is applied. In acne vulgaris, after steaming, **strong sulphur** and **ichthyol soap** is used with **brisk rubbing** with a flesh-glove. Brownlie (N. Y. Lancet, May, 1901).

The following **resorcin** paste is recommended:—

℞ *Resorcin* ..... 2½-5 parts.
Zinc oxide,
Starch .....of each 5 parts.
Vaselin ..... 12½ parts.—M.

This paste may remain on a day and a night and then be removed with a piece of cotton. Cure is said to be speedy, occurring in three or five days. It is a strong preparation, acting with considerable energy in some cases.

> In slight cases of acne of the face the following formula is recommended: **Eau de cologne,** or 90 per cent. **alcohol,** with **resorcin** or **salicylic acid,** 2 to 4 per cent., or **sublimate** or **cyanide of mercury.** After these lotions the skin should be slightly greased with **lanolin,** 10; **water,** 20; and **rose water,** 5 parts. The application of an aqueous solution of **ichthyol,** 5 to 10 per cent., is also useful. Leredde (Bull. gén. de thérap., 1903).

Salicylic acid acts well in from 1 to 2½ per cent. in various ointments.

Electrolysis has been recommended for the removal of the indurated masses left on the skin.

In acne of the back the strongest applications, as a rule, are demanded. Of especial value in some cases is the **liquor calcis sulphuridis (Vleminckx's solution).** This should be used at first diluted.

Massage of the face is not to be commended for acne, often doing distinct harm.

> The comedo is in the majority of cases the forerunner of the acne nodule and pustule. The comedo is best removed by a comedo extractor, which should have rounded edges. The pressure should be moderate, and if the comedo does not escape it is best to

puncture with a narrow bistoury. This should be done by the physician. The papules and pustules are treated by **lancing.** When more active methods are not employed, it is of value to cover the parts with **mercurial plaster** for a few nights. Various useful methods have been devised, the main local applications consisting of **sulphur, salicylic acid, resorcin,** and **soap.** The best treatment, however, is the **X-ray.** In many cases irradiations will obviate the necessity of lancing the nodules and pustules. D. Lieberthal (Lancet-Clinic, Dec. 30, 1905).

Before undertaking the local treatment of acne it is well to **open the pustules, empty the comedones** and sebaceous cysts, etc. These measures often prove satisfactory in indurated and rebellious acne. Some observers object, however, to the use of the curette.

Facial acne gives favorable results under treatment by a **glass vacuum electrode excited by the Oudin resonator** and transmitting quite a strong current. The bulb should be rubbed over the skin without breaking the contact, and at the same time a constant stream of tiny violet sparks should pass from parts of the bulb not in the closest contact with the skin. The face should be somewhat red after an application lasting six or eight minutes during which the electrode is in constant motion. The writer is most strongly opposed to the practice of opening acne pustules. He has seen faces as badly marked as by small-pox. It seems much better to treat the ase along the following lines: **Rhubarb and soda** internally relieve any source of irritation, such as phimosis; cleanse the skin by vigorous **washirg with tar soap** every night and then apply a soothing antiseptic salve, such as **ung. zinci oxidi,** 2 ounces (62 Gm.); **pulv. acidi salicyl.,** 20 grains (1.3 Gm.). This treatment combined with that by **high-frequency currents** has enabled the author to permanently cure a number of cases of acne vulgaris and the disagreeable and intractable acne rosacea. Sinclair Tousey (Amer. Jour. of Dermat., Oct., 1911).

Mild **X-ray** exposures of short duration and low vacuum may often be advantageously employed, but should be done with great caution and as an aid rather than the sole measure of treatment. Its indiscriminate and injudicious use is to be condemned.

Treatment of acne by exposure to the **X-rays** tried in 15 cases. With one exception satisfactory results were obtained. The cases were not selected. R. R. Campbell (Jour. Amer. Med. Assoc., Aug. 9, 1902).

In acne vulgaris which resisted all other forms of treatment, the **X-rays** acted very favorably. It caused absorption of recent papules, and crusting over and disappearance of pustules. The best results were obtained after fairly strong cutaneous reaction took place, as indicated by marked hyperemia and desquamation. The first effect of treatment was to aggravate the condition. As improvement was observed only after the reaction subsided, several applications were necessary to produce a cure. Torok and Shein (Wiener klin. Rundschau, Sept. 13, 1903).

Four cases of acne treated with the **X-ray.** Two were entirely cured, while the other showed very marked improvement and were nearly free from the disorder. The duration of the disease previous to its use varied from sixteen months to two years. The soft tube was used in every case at a distance from six to nine inches, and an exposure of about eight minutes. This was done three times a week, requiring from five to twelve exposures. Slack Atlanta Jour.-Rec. of Med., July, 1903).

In pustular and indurated acne time is usually lost by waiting. Medication will remove comedones and produce desquamation, but it has as little effect on the overactive sebaceous glands as has the **X-ray;** in pustular acne the rays seem to have a fourth action on the staphylococci by rendering the

soil inert. Care must be taken to avoid undesirable results; this is insured by using a very low vacuum tube with the anode at eight inches from the skin, one and a half milliampères of current and from five to ten minutes' exposure, according to the condition of the patient. Nine treatments usually show how much more will be required, and what variations of the treatment are needed. R. H. Boggs (Jour. Amer. Med. Assoc., Aug. 31, 1907).

The **ray treatment** and the passive hyperemia treatment have much in common. The bactericidal effect of the rays lies in their power to increase the local opsonic index just as it is increased by the old treatments. But the rays also bring about a vascular constriction and produce atrophy of the sebaceous glands in which all acne begins. The uncertainty of currents, the variance of tubes, the personal idiosyncrasy of the patient, the factors of knowledge gained by experience on the part of the operators, must all be given weight, and these, collectively, make it impossible to state in any given case what the result, beneficial or harmful, of ray treatment may be. The legal rule is now established by precedent that, if the ray operator possesses and exercises the average knowledge of the treatment, he is not responsible for the injuries that may occur. The patient should always be warned of the dangers of the ray treatment. A. W. Brayton (Jour. Ind. State Med. Assoc., Apr. 15, 1908).

Report of 4 cases of very disfiguring and obstinate acne keloid (dermatitis papillaris capilliti of Kaposi) successfully treated by means of the **X-rays.** It produces in moderate or large doses prompt healing, even in cases which have lasted many years; in some instances a single sitting may be sufficient to bring about the disappearance of the disease. Kienböck (Archiv f. Dermat. u. Syphilis, Bd. xc, H. 3, 1908).

When the lesions are somewhat indurated, the use of the **actinic lamp** twice weekly for periods of from fifteen to thirty minutes has given the writer excellent results as a supporting measure. For the deeper indurations the **X-ray** has proven very useful, and by many dermatologists this is the method of choice. It is, however, in the long run, no more successful than some of the older methods, and should be reserved for those cases which are obstinate to other forms of treatment. The injection of **vaccine** made from dead cultures of the acne bacillus and the staphylococcus, suspended in salt solution, has given good results, and, in the writer's opinion, should be given the preference over the X-ray. The reports of cases treated by vaccine therapy also show it to be a method that is well worthy of a careful trial in rebellious cases. Sampliner (Ohio State Med. Jour., Feb., 1910).

According to Bier, nature always meets a pathogenic substance with the same weapon, namely, **hyperemia.** This is shown either by scratching a sterile skin with a sterile needle or by infecting any organism with any irritating or poisonous germ, or, most commonly of all, by the reaction of the part when a small splinter is lodged in the skin. The object is to increase the blood-supply to the affected or the infected part and by so doing to increase the supply of leucocytes, and by this means either to destroy the infective germs or, by an increase of serum, to dilute the poison till harmless, or to wash away the *débris* or infection. Bier's method has recently been tried in acne with some degree of success.

Bier's method for the treatment of acne consists in the application of dry cups to the affected region for one-half hour once or twice a day. The suction is slight, and the cup is removed and reapplied every one or two minutes. From two to five applications must be made over the same area before improvement is effected. The method does not prevent the appearance of new pustules, though they become less fre-

quent. Eight cases treated by this method alone produced marked improvement. E. Moschowitz (Med. Rec., Jan. 13, 1906).

Bier's suction cups found useful. Applied for repeated five-minute periods with three-minute intervals. Usually two to five applications at each *séance*. Considerable degree of congestion, and frequently repeated treatment, required, first to large affected areas and afterward locally to persistent individual comedones and pustules. Increases local blood-supply, encourages removal of deleterious products, activates sweat-glands, and promotes action of drugs locally applied. Sibley (Lancet, Feb. 4, 1911).

Sir A. E. Wright's **vaccine therapy** has also been used with success in acne. As this investigator explains, no attempt is made to supply to the patient protective substances produced in the organism of an animal vicariously inoculated, but the chemical machinery of the patient is induced to elaborate by its own efforts the protective secretion which is required for the destruction of the pathogenic agent.

Series of cases illustrating the fact that, while in some cases an autogenous vaccine of acne bacillus is necessary, experience has shown that in the vast majority of cases great improvement has been induced by the inoculation of a stock **vaccine** combined with staphylococcus if an examination of films has revealed that the organism is present. The dose used had varied from 4,000,000 to 10,000,000, and the interval between inoculations from one to two weeks. The guide to treatment has been the appearance of fresh lesions, either during the period of low resistance following the positive phase when too long an interval has been allowed to elapse or in the next two or three days after an inoculation indicating that too large a dose has been administered. By watching these signs and working the dose up till it just fails to show any "negative phase" clinically, one obtains the maximum benefit from the vaccine. In this way a large number of cases of acne in all its stages have been greatly improved, and in a fair proportion the lesions have totally disappeared. On cessation of treatment in several instances, especially in some cases where attendance ceased before the condition had entirely disappeared, there was a recrudescence of the disease, which, however, rapidly gave way to subsequent treatment. Alexander Fleming (Lancet, Apr. 10, 1909).

The use of **polyvalent vaccine** (prepared from cultures of staphylococcus albus, citreus and aureus) answers well enough in most cases, especially when there is much pustulation. When the chief feature is the comedo, an acne bacillus vaccine is indicated. A mixed vaccine of 200,000,000 polyvalent staphylococci and 8,000,000 acne bacilli is what has been used by the writer in recent cases. The dose must be gradually increased to the maximum with about ten days' interval, and the effects very carefully watched. He has found the treatment to yield brilliant results in some cases, while in others the condition recurs shortly afterward. Walsh (Med. Press and Circular, Jan. 26, 1910).

The treatment of acne vulgaris with suspensions of **acne bacillus** has proved, in the author's hands, since a proper technique has been adopted, the most brilliant therapeutic agent yet seen in dermatology. Some of the cases respond, as does the membrane in diphtheria, to its antitoxin; nothing else in medicine can compare with its action in favorable cases. There is only one drawback in these very favorable cases, and that is the lesions undergo such complete and rapid involution that deeper and more marked scars supervene. Nothing demonstrates Wright's negative phase better than these suspensions in acne. Invariably two or more new lesions appear within forty-eight hours after the injection. If a large dose is given, a numerous crop can be produced, and the negative phase prolonged for days. By repeated large doses a mild case can be aggravated or converted into a severe one

with large cystic lesions, and, furthermore, the positive phase in such instances is not clinically evident. Such a patient remains for some time extremely sensitive to any dosage. Such has been the writer's experience with doses of 50,000,000 at seven-day intervals, an experience repeated several times by him. Mild cases stand a larger dose than severe ones; in the latter, continuous small doses give the best results. Engman (Interstate Med. Jour., Dec., 1910).

The writer found in 28 successive cases that by painting an acne lesion with old staphylococcus vaccine it healed rapidly. The comedones dried up and were easily removed by rubbing with a coarse towel. Moreover, the large, open pores became constricted, leaving a perfectly normal skin. At first, the application caused redness with a sharp, stinging pain that lasts a few minutes, but these phenomena become less marked as additional applications were made. Le Roy (N. Y. Med. Jour., Dec. 31, 1910).

The writer, experimenting with vaccines derived from the laboratories at St. Mary's Hospital in cases of acne, either simple or complicated by suppuration, and with the addition of no local treatment, found in 9 cases of pustular acne with comedones manifest improvement in the pustulation after the injection of mixed vaccines of microbacillus of acne plus staphylococcus. In 8 cases the effect was almost *nil;* in 3 cases there was temporary aggravation of the pustulation, probably, as the author says, due to too close approximation of dosage; in 2 cases of pure comedo formation there was pronounced improvement. The injection consisted of 5,000,000 to 10,000,000 acne bacillus vaccine every five to ten days, and 125,000,000 to 250,000,000 staphylococcus vaccine every five, ten, or fifteen days. Lassueur (Ann. de Derm. et de Syph., July, 1910).

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ACNE BACTERIN. See BACTERIAL VACCINES.

ACNE ROSACEA.— DEFINITION.—Acne rosacea is characterized by a chronic congestion of the face, causing vascular dilatations; and by changes in the cutaneous glands and tissues, giving rise to seborrhea, inflammatory acne, and hypertrophic changes.

SYMPTOMS.—The nose and malar eminences are especially prone to this disorder. It may also affect the forehead, chin, the neighborhood of the alæ nasi, the cheeks, and less commonly the side of the neck. In women the chin is occasionally invaded.

There are three forms of acne rosacea.

The first is the *erythematous and telangiectasic.* It may be characterized by temporary congestive spots on the face, showing themselves especially after meals and in the evening. These spots may be accompanied by no other lesion. This form is usually present in connection with more or less seborrhea, especially on the nose, which is generally very oily. Again, the erythematous variety may be characterized by small vascular dilatations on the nose or malar eminences, which dilatations develop gradually, unite with one another, and form a network. This network is uniform in hue at a distance, but nearby may be seen to be formed of congested surfaces over which are spread vascular dilatations. This degree of the erythematous form is almost always accompanied by seborrhea, enlarged nose, and dilated glandular orifices, especially in women toward the menopause and in wine-drinkers.

The nose may be slightly violet hued and be cold to the touch.

The second form is the *erythematous* acne, or *true acne rosacea*. In addition to the erythematous and congestive feature, there may be found in this variety a true acneic and acne-like element: papules, pustules and tubercles or nodules. In some cases the acne appears before the congestion. There is a congestive red base with fine vascular dilatations and papulopustules of various sizes, often resting on an indurated violet-red base.

In this variety there may also be increase in number and size of the vascular dilatations, increase in size and depth of the acneic indurations, and proliferation and hypertrophy of the derma.

The third form is the *hypertrophic* acne, or *rhinophyma*. In this variety the glandular orifices are much enlarged, while the glands themselves may be ten to fifteen times increased in size. The tissues around them proliferate, forming a variety of pachyderma. The nose may be red or violet hued, covered with enlarged orifices, greatly increased in size, occasionally reaching considerable dimensions (the so-called Pfundnase of the Germans). Its exterior may be mammillated. (Brocq.)

Two subdivisions of this form are rendered necessary by the difference in the pathology of each. The first, glandular, presents an embossed aspect, the hypertrophy being due especially to hypertrophy of the pilosebaceous glands; the second, elephantiasic, presents a smooth aspect, being due to chronic edema; there are also vascular dilatations, with sclerosis of the derma. (Vidal and Leloir.)

ETIOLOGY.—Women suffer more than men from the erythematotelangiectasic and acneic forms. Men only suffer from hypertrophic acne. It usually appears between 30 and 40 years. In women, rosacea develops usually at from 30 to 45 years, and increases decidedly toward the menopause, after which it may recede. It may also, however, develop at puberty.

In young women and girls acne rosacea is frequently due to chlorosis, dysmenorrhea, or sterility. In some it recurs at each conception.

Some authorities claim that, among the constitutional causes, heredity plays an important part.

Cold feet, urethral and uterine disturbances, and constipation are also recorded as causes of the disease. Exceptionally a factor in acne may be found in the mouth or teeth and be unilateral if the cause is one-sided (E. Besnier, Doyon).

Dyspepsia, neuralgia, hemicrania, working with the head inclined forward, and disease of the nasal fossæ are among the less frequent etiological factors (which affect men more than women), while high heat, overheated rooms, high wind, sea air, cold, and cold water are occasional causes, especially in men. The disease may become started in people who for several years have indulged in excessive hydrotherapeutic treatment. (Kaposi.)

Certain occupations which expose to heat, cold, winds, etc., such as those of coachman, baker, smith, fireman, glass-blower, may also become primary causes of the trouble. Indiscretion in diet and alcoholic beverages are well-known factors. According to Kaposi, in wine-drinkers the nose is bright red, in beer-drinkers it is violet, while in spirit-drinkers it is soft, large, and dark blue.

PATHOLOGY.—The vascular dilatations of the face have been considered by some authorities as due to circula-

tory troubles caused by compression of the veins in the cranial foramina.

A certain paretic condition of the vascular walls may often be looked upon as a cause. (Brocq.)

The cutaneous nerves of the region affected have been found normal by E. Besnier. According to Leloir and Vidal, however, there is congestion of the deeper venous network of the skin; dilatation of the same vessels and of the perifollicular vascular network, their walls being often diminished in thickness. There is also formation of new vessels.

DIAGNOSIS.—Lupus Erythematosus.—The superficial, congestive variety shows a brighter and better defined redness; crusts or squamæ on the surface; sharper and more definite edges; greater sensitiveness to pressure; slight elevation above the surrounding surface. There are no papules, pustules, or tubercles. If any cicatrix be present, it is surely lupus erythematosus.

> Acne telangiectodes is an affection *sui generis,* and not identical with lupus follicularis disseminatus; but it is identical with the acnitis of Barthelemy, and must be distinguished from the disease known as folliculitis. It presents no sort of etiological relationship to tuberculosis, and should be separated from the tuberculomata and the tuberculides. It does not take its origin in the sebaceous glands and, therefore, does not belong to acne. Pick (Archiv f. Dermat. u. Syphilis, Bd. lxxii, H. 2, 1905).

Circumscribed Congestive Seborrhea.—In this disorder there is a limited extent of patches, shallower and more uniform redness, with crusts covering them.

Sycosis Coccogenica.—This is always an inflammatory disease of the hair-follicles and perifollicular tissues. There are numerous papules and pustules, each perforated by a hair, and often capped by a small circular scale. The upper lip and chin are sites of predilection. The affection is usually painful.

Congenital adenoma sebaceum also has a special location: the nasogenial furrow, the parts around the nose, mouth, and chin. It presents a mammillated aspect, and its predilection for early youth and its normal evolution serve to establish its identity.

Eczema.—Erythematous, or pustulopapular, eczema of the face may sometimes present diagnostic difficulties. In this disease, the more or less constant, and usually intense, itching, the serous or seropurulent secretion, and the desquamation will suffice to establish the diagnosis.

Chilblains.—Changeableness of the lesions and pains are peculiar to this disorder.

Acneiform Syphilides.—Here the manner in which the elements are grouped, the long duration of their evolution, their tendency to ulceration, and consecutive cicatrix are important.

Rhinoscleroma.—In this disorder there are hard or ivory-like masses imbedded in the nose.

PROGNOSIS.—Acne rosacea does not always increase; it may remain stationary or even recede, especially in women after the menopause.

TREATMENT.—As to general treatment, it is especially necessary to pay strict attention to the good condition of the stomach and intestines, by appropriate measures and suitable diet. Purgatives are absolutely necessary from time to time; laxatives should frequently be given and constipation should be avoided (Brocq).

> In many cases, especially where the hemoglobin percentage is low or the

bowels are sluggish and irregular, the use of **Startin's mixture** is effective, the formula for which is:—

℞ *Magnesii sulphatis* 30.0
Ferri sulphatis 0.25
Acidi sulphurici diluti 8.0
Sodii chloridi 2.0
Infusi gentianæ ....q. s. ad 120.0

Directions: Take a tablespoonful in half a gobletful of water one hour before each meal, using a glass tube because of the iron. If there is any indigestion this prescription may be alternated with the following:—

℞ *Papain* 8.0
Sodium bicarbonate,
Charcoal .....of each 16.0

Make into 50 tablets. Directions: Two tablets in a wineglassful of hot water before each meal.

J. Philip Kanoky (Amer. Jour. of Clin. Med., Aug., 1908).

Proper circulation of lower limbs should be insured by adequate clothing. Any abnormal condition of the genito-urinary tract or of the upper respiratory tract, especially the nose, should be corrected, while anything tending to cause congestion of the face, such as tight collars or stays, should carefully be avoided. Sedentary intellectual work, especially by gaslight, frequently aggravates these cases.

On the supposition that a rheumatic diathesis is a possible etiological factor, various alkalies have been recommended, especially **bicarbonate of soda** or the various **alkaline waters.**

Where the face is intermittently congested, **quinine, ergotine, belladonna, digitalis,** and **hamamelis** have been suggested. These may be combined in a mixture, with or without the **tincture of aconite-root.** Vasoconstrictor drugs have but little influence.

Perchloride of iron, tannin, ergot, and **tincture of hamamelis** are recommended by E. Besnier and A. Doyon.

The following preparation is extolled by Brocq:—

℞ *Quinine hydrobromate,*
Ergotine .....of each 30 grs.
Belladonna extract ..... 6-12 grs.
Lithium benzoate ..... 30 grs.
Excipient and *glycerin*..... q. s.

Misce. For forty pills.

Sig.: Two before each of the two principal meals.

Rhubarb or **aloes** may also be added if necessary.

The local therapeutic agents are the same as in acne vulgaris; though some irritable varieties of acne rosacea exist, it is usually necessary to act with greater energy.

Hot water and **mercurial preparations** are often of value. Mercurials are, however, much inferior to the sulphur preparations.

The following has been employed by Bazin with success:—

℞ *Mercury biniodide* ..... 7½-15 grs.
Lard ..... 1 oz.—M.

Sulphur preparations, as already stated, are, however, the most useful, those commonly employed in acne being prescribed.

In cases of average intensity dermatologists frequently employ **Vleminckx's solution,** at first with 5 parts of water, then gradually making it stronger until it is used pure. It should be left on several minutes, and followed by very hot water; it may often be left on overnight with advantage.

Green soap gives the best results in obstinate acne rosacea, alone or when used in conjunction with **sulphur, naphthol,** or **salicylic acid.** It may be used as in acne vulgaris or spread on a piece of flannel; the latter is then cut out to fit the affected region, and left on as long as possible. It should not be left on too long. When the irrita-

tion becomes too great, the application should cease and cooling preparations, such as the following, be used:—

℞ *Salicylic acid* ..... 7 grs.
Zinc oxide,
Bismuth subnit. .....of each 30 grs.
Lycopodium ..... ½ dr.
Vaselin ..... 2 drs.
Lanolin ..... 3 drs.

Ichthyol does not seem to be as efficacious in acne rosacea as in some other varieties of acne. (Brocq.)

Unna recommends daily doses of 7½ grains of **ichthyol** internally and lotions with ichthyol dissolved in water, washing with ichthyol soap. **Steam** or **sulphur-water douches** have also been used with good results.

A solution of **iodine in glycerin,** applied twice daily during three or four days, is recommended by Kaposi for the more severe forms, but it is disfiguring and not advisable for patients outside of hospital wards.

The commencing erythema of acne rosacea, a very troublesome and disfiguring complaint, especially to ladies, is removed by an ointment containing 10 grains of the **iodide of cadmium** in 1 ounce of **vaselin.** It should be rubbed well into cheeks and nose at night, and washed off next morning with **hot water** and an **overfatted soap,** accompanied by **massage** of all the affected skin. The iodide of cadmium does not stain the skin and is an excellent local stimulant. If too strong it irritates. H. S. Purdon (Dublin Jour. of Med. Sci., Sept. 1, 1903).

In a series of cases of acne rosacea the author succeeded in gradually removing the eruption by means of painting with undiluted **iron chloride.** The applications were repeated every morning and evening, and resulted in a complete cure. A somewhat solid crust is apt to form at the end of four or five days, and the paintings should be omitted until this crust is cast off spontaneously. When there is much tension the surface may be covered with a clean rag that has been thickly spread with **Wilson's salve** or some other suitable ointment. In the presence of severe inflammation an **ice-bag** may be applied. As a rule, frequent interruptions are unavoidable, and the treatment is therefore likely to last about three or four months, until the cure is complete. Zeissl (Münch. med. Woch., Nu. 20, 1908).

Surgical treatment in this disease is the most efficacious. (Brocq.)

Electrolysis is another satisfactory method. A fine platinum needle is inserted alongside of the vessel, and, if possible, into it, and connected with the negative pole, while the patient holds in his hand a cylinder in communication with the positive pole. A large eschar must be avoided. (Hardaway.)

Electrolysis of each dilated sebaceous follicle with a negative platinum needle and a current of from 4 to 6 milliampères is an effective, though tedious, measure. The needle should be moved around in the follicle in order to thoroughly destroy it.

In the early stages of acne hypertrophica, **diet,** a local spray of **sulphur lotion,** and **electrolysis** of the enlarged sebaceous glands are sufficient. But when hypertrophy occurs, with deformity and tumors of the nose, surgical measures only are satisfactory. The author prefers **thermocautery** to the knife, and considers grafting undesirable if this is used. When the knife, however, is used, **skin grafting** may hasten recovery and prevent cicatricial contraction. Dubreuilh (Ann. de Derm. et de Syph., Nov., 1903).

The ordinary **galvanic** or **faradic currents** have been recommended by Cheadle and Piffard.

Scarification was formerly a favorite method. The best instrument is Vidal's ordinary scarificator. The skin is cut obliquely or perpendicularly to the

vessels, then slightly obliquely across these so as to form lozenges, and as near together as possible (from 1 to 1½ mm. apart), and not deep enough to penetrate entirely through the dermis, so as to avoid cicatrices.

> If there are only a few large veins visible at the root of the nose, the writer merely pierces each of these with a **galvanocautery** needle; but if there are many he punctures the entire skin of the nose with points so close together that no vessel can be missed, to a depth of ½ to 1½ mm. The entire skin soon sloughs off, and the resulting raw surface is trimmed into shape as necessary by the cautery, and dressed with an antiseptic powder (**bismuth, dermatol**). The skin heals in about twelve days. This method has given better results than operations with the knife or electrolysis. Bolebaum (Münch. med. Woch., No. 52, 1904).

An hour afterward the part is washed with a **corrosive sublimate solution**, 1 : 1000; then in the evening or the following day compresses dipped into an **ammonium hydrochlorate solution**, 1 : 100, or **corrosive sublimate**, 1 : 500, are applied. If too strong, warm water is to be added. If the reaction is too violent, **starch poultices, bland pomatums**, or **zinc oxide plasters** can be employed.

The treatment should be renewed in from five to eight days. Amelioration will occur in from eight to ten sessions, and marked improvement in from fifteen to twenty-five sessions.

Scarifying should be begun in the lower part of the region to be operated upon, in order not to be troubled by the blood covering the surface. (E. Besnier, A. Doyon.)

In the early stage of hypertrophic acne the scarification must be made deeper, and in many cases it is essential to also **cauterize** the glands deeply.

In the advanced hypertrophic form direct **removal with the knife** is the best procedure. (Brocq.)

> In hypertrophic acne of the nose the writer recommends **ablation** with knife and scissors under cocaine anesthesia. The disease is really an adenoma of the sebaceous glands of the nose, and in spite of appearances is confined to the skin and its annexes, and always ceases at the margins of the nostrils. The tumor is divided vertically into two halves; each half is separated from the margin of the nostrils, and an incision is made outside beyond the limits of the growth. The two halves are then successively removed *en bloc* or by repeated sections. The bleeding is abundant, but is, as a rule, easily controlled by pressure or by forceps. Care must be taken not to injure the fibrocartilaginous framework of the nose. It is better not to graft the wound with skin or do any autoplastic operation. In five or six weeks the skin has grown over and covered the wound. If the wound is not being covered quickly enough, grafts may be applied when granulations are abundant. Morestin (Arch. gén. de méd., vol. cxcii, p. 2330, 1903).

Hypodermic injections of alcohol have recently been recommended. **Phototherapy** has likewise given satisfactory results; both **high-frequency current** and the **X-ray** are of value in some cases.

> The **light treatment** of this form of acne should be included among the recognized therapeutical measures. It brings about a cure more rapidly than chemical means (salves, etc.), and is more quickly efficacious than it is in tuberculous or erythematous lupus. In most of the cases the cure remained perfect; in others it became so when combined with external treatment, and with the necessary attention to the visceral disturbances, especially of the gastrointestinal tract. **Phototherapy** is specially applicable to rosaceous acne of the nose, where the lesions are often

much deeper than on the cheeks; but if the action of the light is not promptly efficacious, scarification may be used at the same time. M. Leredde (Jour. des praticiens, April 18, 1903).

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ACNE VACCINE. See BACTERIAL VACCINES.

ACOIN, a synthetic compound used as local anesthetic, especially in dental and ophthalmic practice. It is designated as alkyloxyphenylguanidin and occurs as a white crystalline powder, readily soluble in pure cold water to the extent of 6 per cent., and in alcohol.

A 1:200 aqueous solution injected under the skin causes a local anesthesia lasting about one hour. Acoin presents the drawback, however, of being quite unstable, while producing greater irritation than cocaine, and is liable to produce necrosis. S.

ACONITE.—The preparations of aconite usually employed are obtained from the root of the *Aconitum napellus* (monkshood, wolfsbane), a conical tuber greatly resembling horse-radish. This resemblance has caused many deaths. Aconite-root is, however, brown in color, and when scraped does not emit the pungent odor peculiar to horse-radish. Again, instead of irritating the palate, as does horse-radish, aconite-root, when masticated, soon produces in the mouth a sense of warmth and tingling, soon followed by local numbness varying in duration according to the length of time the mucous membrane is exposed to the effects of the drug. Aconite owes its activity mainly to the alkaloid aconitine, of which the dried root is officially required to contain 0.5 per cent.

PREPARATIONS AND DOSE.—Aconite in substance is not employed, and the preparations made with the leaves are no longer official.

The tincture (*tinctura aconiti,* 1905 U. S. P.) is no longer stronger than the English or French tinctures. It is a 10 per cent. tincture, *i.e.,* it contains 10 Gm. of the drug in 100 c.c. *Dose,* 3 to 10 minims, every three hours. Its effects should be closely watched, especially in anemic and corpulent individuals and in those addicted to alcohol. In prescribing the tincture, the 1905 U. S. P. should be specified, to avoid accidents.

The fluidextract (*fluidextractum aconiti,* U. S. P.), ½ to 1 minim.

The alkaloid aconitine (*aconitina,* U. S. P.), $\frac{1}{600}$ grain to $\frac{1}{300}$ grain (0.1 to 0.2 mg.), occurs in the form of colorless tabular crystals slightly soluble in water, but soluble in alcohol, ether, and chloroform.

Aconitine is a very active poison and causes the responsibility of the physician to be involved to a greater degree than any other toxic. Its activity is markedly increased when it is administered hypodermically, and the injections are very painful. These facts and the variations in strength of the various aconitines on the market have militated against its use, and it is best to utilize the other preparations, both of which owe their activity to aconitine.

MODES OF ADMINISTRATION.—Internally aconite is usually better given in small and frequently repeated doses than in large doses at longer intervals. Thus the tincture may be given in 1 minim doses every hour until the desired effect has appeared or until distinct depression of the circulation indicates cessation of the drug. Aconite should be administered well diluted. In fever a dram of a mixture of 10 minims of the tincture in 4 ounces of water may be given every fifteen or twenty minutes. For the relief of pain,

5 minims may be administered as the first dose, smaller ones being then given at short intervals. For **cardiac overactivity,** doses of 2 to 5 minims (0.12 to 0.30 c.c.) may be given thrice daily. When aconite is used over a long period, a gradual increase in its action is observed. Even where indicated, aconite should not be given freely with the intention of producing powerful effects, as its action in large doses is sometimes unexpectedly severe.

Aconitine may be administered internally in granules, in tablets or tablet triturates such as are official in the N. F., or in solution in water (1 in 3200). Tison has used aconitine nitrate dissolved in a mixture of distilled water, alcohol and glycerin, 1 minim of the solution containing $\frac{1}{3200}$ grain of the salt. As stated above the alkaloid should be employed with great caution, as individual intolerance of it has been repeatedly observed; a third dose of $\frac{1}{130}$ grain (0.5 mg.) has been known to cause death (Lépine). Dose of $\frac{1}{1300}$ grain (0.1 mg.) may be given every two or three hours, the drug being stopped when the first signs of toxic action appear; these are, according to Gubler: prickling of the tongue, a sensation of shrinkage in the face, and loss of elasticity of the muscular openings in this region. These are followed by general numbness and chilliness. A total amount of $\frac{1}{100}$ to $\frac{1}{65}$ grain (0.66 to 1.0 mg.) in twenty-four hours may be considered the limit of safety. Dujardin-Beaumetz advised never to give aconitine unless its effects can be carefully watched.

LOCAL USE.—Aconite is used locally in neuralgia and skin affections, the tincture sometimes diluted with alcohol, or the linimentum aconiti et chloroformi of the N. F. (fluidext. aconit. 4.5, chloroform 12.5, in alcohol 100), being applied. The alkaloid is also sometimes used in a 2 per cent. ointment or in the oleatum aconitinæ, N. F. (2 per cent.), but should never be applied to abraded areas. Undiluted aconitine is absorbed through both mucous membranes and skin to a considerable extent.

Subcutaneous injections of aconitine have been given for *neuralgia,* but the pain caused and the danger from prompt toxic effects are marked disadvantages.

INCOMPATIBILITIES.—The alkaloid aconitine in solution (1 to 3200 being saturated) is incompatible with tannic acid, gallic acid, mercurials, and Lugol's solution; aconitine nitrate is precipitated as the alkaloid by alkalies. Among the physiological incompatibilities of aconite may be mentioned digitalis, atropine, strychnine, strophanthus, ammonia and alcohol.

CONTRAINDICATIONS. — By reason of its depressant action aconite is contraindicated in all cases in which prostration exists or threatens. If the respiration is embarrassed; if the heart is in asystole; if the patient is depressed, recourse must be had to tonics and stimulants. In bronchopneumonia, pneumonia after the primary stage, typhoid fever, phthisis, valvular affections of the heart, and in all cases of collapse occurring in acute infectious diseases, aconite is particularly contraindicated. In no case where the heart is weakened or degenerated should the use of aconite be considered. Old age contraindicates its use to lower the blood-pressure in nephritis.

PHYSIOLOGICAL ACTION. — Within half an hour after its administration, aconite commences to affect the general system, slowing and weak-

ening the heart's action, lowering arterial tension, increasing the action of the skin and kidneys, and producing more or less muscular weakness in proportion to the amount taken. It causes a tingling sensation in the lips, extremities, and, perhaps, the whole body; it diminishes the rapidity and depth of the respiration, and causes disorders of vision, vertigo, and loss of tactile sensibility and sense of pain. The effects of a therapeutic dose last three or four hours.

Aconite, when administered in sufficient dose, is a powerful depressant of the sensory nerve; some have believed that the stage of nerve paralysis is preceded by one of nerve stimulation, but Wood considers this doubtful. The drug paralyzes first the sensory end-organs, next the nerve-trunks, and finally the centers of sensation in the cord. The reflexes are correspondingly impaired. The power of voluntary movement, which continues after the cessation of the reflex functions, is finally lost, owing to the later action on the motor centers of the cord, and subsequently on the nerve-trunks. The brain is practically unaffected by aconite.

Laborde and Duquesnel state that aconitine in therapeutic doses has a particular effect in modifying special sensibility in the area of the trigeminal; they believe this effect to be exerted on the bulbar receptive nuclei of the nerve. According to Cushny, the subjective sensory phenomena resulting from the use of aconitine are due to a marked primary stimulation and secondary depression of the sensory end-organs, tingling and warmth locally being followed by numbness when the drug is applied to the skin or taken by the mouth.

Pyraconitine, obtained from aconitine by heating to separate a molecule of acetic acid, causes no tingling of the lips or tongue. It causes slowing of the heart, partly from vagus irritation, partly from depression in function of intrinsic rhythmical and motor mechanisms. After its administration activity of respiration is reduced (by central depression) to a degree incompatible with life. Neither muscular nor intramuscular nervous tissue is strongly influenced by pyraconitine, but the spinal cord is impaired in its reflex function, and there is a curious condition of exaggerated motility. Theodore Cash and W. K. Dunstan (Brit. Med. Jour., Aug. 17, 1901).

The physiological actions of aconite and veratrum viride are so similar that what is to be said of aconite can be applied with equal force to veratrum. The physiological action of aconite may be stated thus: Primary action: stimulation of the peripheral nerve-endings; stimulation of the vasomotor mechanism; powerful stimulation of the respiratory center. Secondary action: paralysis of the overstimulated peripheral nerve-endings; pronounced depression of the heart; lowering of the blood-pressure; reduction of temperature. W. B. Hill (Jour. Amer. Med. Assoc., Dec. 12, 1903).

When aconite is applied directly to the heart, the number and force of the beats are lessened, and its action is finally arrested in diastole. It lowers the blood-pressure and pulse-rate when given internally by a direct depressant action on the heart itself, and also by stimulating the cardioinhibitory center. Laborde found, however, that the contractility of the cardiac muscle-fiber itself was not directly modified by aconitine.

Hare has called attention to the fact that the fall in pulse-rate from poisonous doses is sometimes preceded by a quickening due to a condition of weakness and abortive cardiac action.

The stage of low pulse-rate is also followed by one in which the pulse is frequent and irregular. Upon the vasomotor center aconite is believed by Cash and Dunstan to have a late depressant effect. It also causes slowing of the respiration, with lengthening of the expiratory period, by depressing powerfully the respiratory center. According to some observers, small amounts of the drug produce, instead, stimulation of the respiratory function, while Cushny is of the opinion that aconitine has a primary exciting effect on most of the medullary centers—vagal, vasomotor, respiratory—as well as the spinal motor centers.

Aconite reduces the temperature both in health and in febrile conditions, probably through an action on the nervous heat-regulating mechanism, and by the circulatory depression it causes. It also increases the action of the skin, kidneys, and salivary glands. Increase of the gastrointestinal and biliary secretions is stated to have occurred. (Schroff, Rabuteau.)

[Personal researches (see "Internal Secretions," p. 1347) have shown that the physiological effects of aconite are due to its depressing action on the sympathetic center, which, as I have pointed out (*ibid.*, p. 1185), governs the caliber of all arterioles. These vessels being thus caused to relax, more blood is admitted into all capillaries, and passive hyperemia of all tissues is produced. If this is slight only a feeling of warmth is experienced; if it is marked the cutaneous sensory nervous elements are sufficiently congested to awaken sensations of prickling and tingling.

If the dose is large the dilatation of the arterioles is sufficient to reduce markedly the *vis a tergo* motion of the blood in the tissues, and, the rate of metabolism being slowed, the functions of the tissues are inhibited; hence the lowered temperature, the numbness, and, if the dose is large enough, the paralysis. C. E. DE M. S.]

MODE OF ELIMINATION. — Aconite is excreted mainly by the urinary organs, though it has also been detected in small amounts in the saliva and the bile.

ACONITE POISONING. — The symptoms following the ingestion of a poisonous dose usually show themselves after a few minutes. The characteristic tingling, prickling, and subsequent numbness already mentioned rapidly extend from the mouth and fauces to the face, thence to the body and extremities. Great prostration and muscular impotency follow. Speaking requires marked effort. The skin becomes cold and clammy, the perspiration covering the surface, and the tissues communicating to the hand an icy coldness. Muscular pains may be present in the early stages, especially in the face. There is often experienced marked epigastric pain with nausea and vomiting. Later on the nausea ceases, owing to paralysis of the stomach walls.

The heart-beats are greatly reduced in number and power. The pulse is usually irregular, compressible, slow, and so weak, at times, as hardly to be palpable; in the advanced stages, however, it becomes abnormally frequent. The breathing is labored, irregular, and shallow, the number of respirations being at first decreased, then increased. Cyanosis may appear. The temperature is lowered, sometimes considerably.

The pupils may become dilated or remain of normal size and react equally; occasionally they are contracted. According to Manquat, they undergo frequent variations in size at first, then dilate. The eyes may protrude or be shrunken; therefore they afford no differential information as to the nature of the drug used.

The mind is usually clear, and the

patient calm, though apprehensive of impending death. Disturbances of vision (diplopia, amblyopia) and of hearing (tinnitus, deafness), as well as vertigo, are frequently complained of. Occasionally epileptoid convulsions occur. Spasmodic purging, with rectal tenesmus and bloody stools, is occasionally present.

Aconite causes paralysis of respiration and circulation, death being due to sudden arrest of the heart in diastole.

[These toxic phenomena are readily accounted for by the interpretation of the action of aconite I have submitted above. The inhibition of function due to the dilated arterioles and the resulting delay in the arterial circulation in the muscles explain, when sufficiently marked, the great prostration, the muscular impotence, the cold and clammy skin, the cold sweats, the relaxation of the stomach walls, the slow compressible pulse (owing to weakness of the cardiac muscle), etc.

The vascular interference with the propulsion of blood to the air-cells and the weakness of the respiratory thoracic muscles account for the intense dyspnea and the shallow breathing. The cause of the failure of respiration is obvious under these conditions, while the cardiac arrest in diastole points to muscular impotence of the myocardium in common with all other muscles. C. E. DE M. S.]

Cases of criminal poisoning by aconite are rare. In the Condon case, of Springfield, Mass., the defendant purchased a two-ounce bottle of tincture of aconite, one-half of which was placed in a pint bottle of port wine and sent to the person whose life was attempted, and who drank nearly one-half of the wine. The immediate effect was dizziness, inability to move, and a peculiar creeping sensation in the muscles. The vision became obscure. Life was only saved by three hours of untiring efforts. W. S. Magill (Med. News, May 31, 1902).

Case of aconite poisoning in which the patient's condition became critical; the pulse varied from 130 to 140, was extremely feeble, and at times was felt with difficulty; the extremities were cold and the lips blue, but the face retained a dusky flush; the convulsive movements were increasing. It seemed clear that the aconite was causing extreme depression of the heart. The writer gave 10 minims of liquid **strychnine** hypodermically and injected 8 ounces of **hot, strong coffee** slowly **into the rectum,** applied **hot bottles,** and wrapped him up in **hot blankets.** After about an hour, during which his condition gave rise to great anxiety, he began to rally, became semiconscious, and rambled in his speech; the convulsive movements gradually ceased and the pulse became fuller and stronger and the body surface warm. At 3 A.M. his condition had so far improved that he was left in charge of a nurse. The next morning he was better, the pulse, though still rapid, was of good quality, and, beyond being somewhat dazed and shaken, he expressed himself as feeling very well, and refused to believe that anything serious had happened. For the next few days, during which his only complaint was of numbness and tingling in the fingers, he was kept at rest in bed until his circulation had resumed its usual state, which showed itself to be one of high tension, bounding vessels, and hypertrophied heart. His recollection gradually came back of having noticed a pungent taste with tingling of the mouth after taking his medicine, but he thought nothing of it at the time, nor did it occur to him that he had made any mistake, *i.e.,* that of taking a tablespoonful of a liniment containing aconite. The quantities contained in the tablespoonful dose of the liniment were 40 minims each of lin. aconiti, lin. belladonnæ, lin. chloroformi, and tinct. capsici, with 80 minims of ol. gaultheriæ. Taking the recognized standard for aconite root as containing 0.5 per cent. of aconitine, 40 minims of lin. aconiti would be equivalent to 0.132 grain aconitine—*i.e.,* about ⅛ grain, or 31 times the maximum dose, which is

given as $\frac{1}{250}$ grain. W. Edgecombe (Lancet, Oct. 29, 1910).

Case of aconite poisoning in a woman aged 45 years, a multipara, who had suffered from rheumatism, shortness of breath, and swollen feet. She drank by mistake about 3 ounces of a liniment. At once she recognized her mistake and experienced a hot tingling in the mouth, then numbness, giddiness, gastric pains, and soon thereafter followed by collapse. A druggist gave ipecacuanha wine and a strong emetic. Sickness continued, and a violent attack of clonic convulsions supervened.

The medical man called in found the patient speechless, cold, pale, skin moist, pulseless, respirations very faint and irregular, and the pupils dilated and insensitive, but no ptosis. The temperature was 96.6° F. Terrible gastric and abdominal pains and violent irritation and prickling of the skin were succeeded by numbness. Three times after attacks of clonic convulsions she appeared dead, but when they ceased the mind was clear and unaffected. As a cardiac depressant, **ipecacuanha** had been given; a **mustard emetic** was now administered to save the enfeebled heart. The head was kept low, the feet were raised, a sinapism was placed over the heart, and hot bottles and flannels were applied to the lower extremities and abdomen. **Strychnine** and **digitalis** were given hypodermically, and **brandy** was injected per rectum. **Artificial respiration** was unceasingly kept up. After an anxious six hours the breathing became stronger, an irregular, intermitting pulse could be felt at the wrist, while the body warmth slowly returned. A little coffee and brandy were swallowed and retained. The crisis passed, and she recovered. The quantity of aconite taken may be roughly estimated as sufficient to kill 6 persons. Inglis (Lancet, Jan. 21, 1911).

Death occurs in from one-half to five and half hours, the average being, according to Reichert, three and one-third hours.

The symptoms resulting from a poisonous dose of the alkaloid aconitine are the same as mentioned above, but they occur more rapidly; hypodermically administered, aconitine may cause death in less than a minute.

Treatment of Aconite Poisoning.—Death in these cases usually follows exertion by the patient. He should, therefore, be kept perfectly motionless in the recumbent position, even during emesis, his head being slightly turned and the dejections received on a towel. An important feature of the treatment is to keep the patient as warm as possible by means of **warm blankets** and **hot-water bottles**, taking care not to place the latter against the skin. The head should also be kept warm. If the patient is seen early the **stomach-tube** should be used at once to empty the stomach. If no stomach-tube be at hand, **apomorphine**, $\frac{1}{12}$ to $\frac{1}{6}$ grain, should be administered hypodermically, or some other active **emetic**, such as **zinc sulphate**, 15 to 30 grains, be given by the mouth.

[From my viewpoint, apomorphine *(q. v.)* is contraindicated as an emetic in these cases, since it causes emesis precisely in the same way as aconite does it, *i.e.*, by depressing the sympathetic center. The emetics which are indicated when there is any degree of depression are, mustard, zinc sulphate, etc. C. E. DE M. S.]

Digitalis, sulphate of strychnine, and **belladonna** are the most effective remedies, but **ether** and **ammonia** should first be employed, owing to their great diffusibility. All these remedies should be used hypodermically, the stomach being unable to perform its functions. A dram of ether, ammonia, **brandy,** or **whisky** should at once be injected, and, after a few minutes, tincture of digitalis, 15 minims; strychnine sulphate, $\frac{1}{20}$ grain; or tincture of belladonna, 10

minims, according to what the practitioner may have. **Atropine** has been recommended as the most powerful antagonist to the depressing effects of aconite on the circulation and respiration. The dosage should be regulated so as to reach the point of physiological action by frequently repeated doses. **Nitrite of amyl** may be given by inhalation, and warm, very **strong coffee** be injected into the rectum.

[Nitrite of amyl, according to my views (see "Internal Secretions," p. 1350), is also a paralyzant of the sympathetic center, and should not be used any more than any other nitrite.

Belladonna I regard as the direct antidote of aconite, since, as stated (1907) in "Internal Secretions," p. 1210, it stimulates "(1) the test-organ (anterior pituitary) and through it the adrenal center, and (2) the sympathetic center (posterior), which governs the tonus and propulsive activity of the arterioles." In other words, it counteracts precisely the paralysis of the sympathetic center caused by aconite. This proves true practically. C. E. DE M. S.]

Case illustrating the physiologic antagonism between aconite and belladonna. The patient had taken by mistake half an ounce of a liniment composed of chloroform, aconite, and belladonna. This means 53.3 grains of aconite root, which represents ¼ grain of aconitine, of which $\frac{1}{16}$ grain has been known to be fatal. He also swallowed 40 minims of fluidextract of belladonna (B. P.), which is equal to 0.3 grain of the total alkaloids. This would represent, approximately, thirty times the official dose of atropine. Of chloroform he took 40 minims, about eight times the official dose. The interest in the case lies in the fact that the lethal effect of a large dose of aconite was abolished by the simultaneous action of a large dose of belladonna. Muscular weakness, numbness of the extremities, and tendency to complete collapse were the only purely aconite symptoms observed. Salivation, which is usually present in aconite poisoning, was absent, and the usually contracted pupil was overcome by the action of the atropine. Finally, the intensely depressant action of aconite on the central nervous system was counteracted by the stimulating influence of the belladonna. The obvious lesson to be drawn from the case is the great value which should be attached to hypodermic injections of **atropine** in aconite poisoning. Speirs (Brit. Med. Jour., Aug. 15, 1908).

Tannic acid is useful as an antidote. Wood recommends that it be followed by an emetic and cathartic to avoid the effects of resolution of the poison by the digestive fluids.

If the patient is seen when the stage of depression has begun through absorption of the poison, the **stomach-pump**, gently used, is alone permissible, emetics at this stage being liable to cause arrest of the heart's action. Tincture of **digitalis**, in 20-minim doses, should be injected hypodermically and repeated as required, besides the other measures indicated. **Frictions** under cover, the rubbing being directed over the heart, serve a useful purpose. **Artificial respiration** is of marked benefit and should be used persistently as long as any indication exists.

Since the strength of the tincture has been decreased (U. S. P. 1905), the cases of poisoning have been greatly reduced, and are seldom in fact met with in literature. Hence the fact that practically all the instances recorded in these pages antedate the year of the last Pharmacopœia.

Twenty cases, 6 of which were fatal, found in the literature of ten years:—

Case 1. Tincture, 7 drams. Recovery. **Emetics; morphine,** ½ grain; **fluidextract of digitalis,** 6 drops; **strychnine sulphate,** $\frac{1}{160}$ grain; **brandy,** 1 ounce; all hypodermically. By the mouth, 2 gallons of **warm water**; fluid-

extract of **digitalis,** 20 drops; **coffee,** 11 pints; **whisky,** 3 pints; **extract of nux vomica,** ½ fluidram; **port wine,** ½ pint. P. F. Brick (Jour. Amer. Med. Assoc., vol. viii, p. 567, 1887).

Case 2. About 8 drops of concentrated fluidextract. Recovery. **Emetics,** coffee, whisky (dessertspoonful). **Heat. Friction** and **sinapism.** T. H. P. Baker (Amer. Pract. and News, vol. iv, N. S., p. 122, 1887).

Case 3. Fleming's tincture, 1½ ounces. Recovery. Emetics, brandy, ether, digitalis, **ammonia carbonate. Amyl nitrite** and warmth. C. C. Bradley (N. Y. Med. Record, vol. xxxii, p. 155, 1887).

Case 4. Tincture, ½ ounce. Recovery. Brandy by mouth and hypodermically. **Ether.** One quart of cold, black coffee. Heat and posture. S. Barnett (N. Y. Med. Record, vol. xxxii, p. 761, 1887).

Case 5. Amount not known. Patient intoxicated at the time. Symptoms of acute poisoning. Recovery. Emetics, brandy, ammonia, and digitalis by the mouth. Sixty minims of tincture of digitalis hypodermically. Heat. Clara T. Dercum (Med. and Surg. Reporter, vol. lxi, p. 1889).

Case 6. Tincture, amount not known. Child, 16 months. Marked toxic symptoms. Recovery. Brandy and fluidextract of digitalis frequently repeated in spite of vomiting. Byron F. Dawson (Med. and Surg. Reporter, vol. lxii, p. 7, 1890).

Case 7. Tincture, 2 drams. Death. Benjamin Edson (N. Y. Med. Record, vol. xxxviii, p. 365, 1890).

Cases 8, 9, and 10. Dr. Edson mentions certain other cases known of, but not treated by him, three of which died. The amounts taken in these were from 1 to 4 drams.

Case 11. Tincture (B. P.), 1 ounce. Death in sixty-five minutes. **Mustard, lavage,** heat, ether, and brandy subcutaneously. L. M. Whannel (Brit. Med. Jour., vol. ii, p. 791, 1890).

Case 12. Fleming's tincture, 1 dram. Recovery. **Sulphate of zinc,** tincture of digitalis, 20 minims hypodermically. Whisky, 1 ounce, by the mouth, followed by **calomel,** 8 grains. L. M. Whannel (Brit. Med. Jour., vol. ii, p. 791, 1890).

Case 13. Fleming's tincture, 1 teaspoonful. Recovery. Mustard, **spirit of ammonia comp.** (B. P.), **tincture of belladonna,** brandy. T. F. H. Smith (Brit. Med. Jour., vol. i, p. 1109, 1893).

Case 14. Fluidextract, 4 drams. Recovery. Emetics, **atropine,** and brandy subcutaneously. Henri E. R. Altenloh (N. Y. Med. Jour., vol. lxvii, p. 358, 1893).

Case 15. Tincture, 7½ drams. Recovery. Mustard, digitalis, and brandy subcutaneously; digitalis, **nux vomica,** and brandy by rectum; ether and ammonia by inhalation; brandy and ammonia carbonate by mouth later. G. H. Tuttle (Boston Med. and Surg. Jour., vol. xxv, p. 678, 1891).

Case 16. Mentioned by, but not seen by, Dr. Tuttle. Tincture, 5½ drams. Death. G. H. Tuttle (Boston Med. and Surg. Jour., vol. xxv, p. 678, 1891).

Case 17. Preparation not noted. Four teaspoonfuls. Recovery. **Sulphate of copper,** digitalis, wine by mouth; whisky by rectum; whisky, $\frac{1}{25}$ grain **strychnine,** and **digitalin,** $\frac{1}{50}$ grain, hypodermically. M. A. Warriner (N. Y. Med. Record, vol. xxxix, p. 521, 1891).

Case 18. Tincture, 2 drams. Recovery. **Apomorphine, stomach-tube,** tincture of digitalis, 25 minims; **aromatic spirit of ammonia,** 45 minims; brandy, 2 drams subcutaneously, heaters, sinapism to precordia. S. Q. Robinson (Boston Med. and Surg. Jour., p. 192, 1892).

Case 19. Tincture (B. P.), 30 minims. Recovery. **Salt and water** one and a half hours after poison. Sulphate of zinc two hours after poison. **Charcoal,** brandy, and water by mouth. William Hardman (Brit. Med. Jour., p. 1893).

Case 20. Preparation not stated. Five drops. Recovery. Belladonna and **strophanthus, champagne,** brandy, heaters. J. D. Leigh (Edinburgh Med. Jour., vol. xl, p. 638, 1895).

Reported by R. W. Greenleaf (Boston Med. and Surg. Jour., July 15, 1897). [The tincture of aconite referred to is that of the old U. S. P.—Ed.]

Case of a man, aged 26, who drank about three-fourths of an ounce of the tincture of aconite. He immediately discovered his mistake, and took about a tablespoonful of ground mustard in water, but could not vomit. The writer administered cider vinegar about fifteen minutes after drinking the aconite. He drank about a half-pint and another half-pint out of a quart jar. In less than five minutes he was greatly relieved, and his pulse was much better. The vinegar almost immediately relieved the burning and choking sensation in his throat. His saliva, which was thick and stringy (hanging down three or four feet, at the writer's arrival, on his attempt to spit), did not change its character for at least half an hour. It gradually became normal. All the symptoms gradually subsided. C. M. Swincle (Homeo. Recorder, Oct. 15, 1908).

[The best remedies used in the cases collected by Dr. Greenleaf were, from my viewpoint, besides **belladonna: digitalis, strychnine, coffee, ether,** and **strophanthus,** all of which, though indirectly in most instances, tend to stimulate the sympathetic center. Morphine, used by Dr. Brick, excites directly the sympathetic center (as do the coal-tar products), but not, as does belladonna, in such a way as to restore the propulsive activity of the arterioles.

Dr. Swincle's successful use of vinegar is of special interest in view of the fact that, as stated in the section on Acetic Acid (this volume, p. 229), I ascribe the toxic action of this agent to reflex excitation of the sympathetic center. C. E. de M. S.]

THERAPEUTICS. — Aconite is mainly used as a **circulatory sedative.** It lessens the blood-pressure by diminishing the force and rapidity of the heart's action, and is, therefore, indicated where a frequent and tense pulse is associated with excessive cardiac activity. It also tends to **counteract spasm** and relieve undue excitability of the nerve-centers, though its property of depressing the cutaneous sensory nerve-terminals is more marked, and is frequently availed of in neuralgic affections.

Aconite causing **increased respiration,** it is indicated where, with a high pulse, there is dryness of the skin. The evaporation of sweat from the surface and the heat radiation due to the increased peripheral circulation resulting from relaxation of the cutaneous capillaries also cause a **reduction of temperature.** Aconite also possesses **diuretic** properties. Hence it appears to be endowed with all the qualities requisite in the incipient stage of uncomplicated inflammatory disorders, as an anodyne sedative.

In children aconite may be given whenever the spasmodic element is clearly marked: in fever preceding attacks of **quinsy, pharyngitis,** etc.; in **asthma** and the asthmatic crises of bronchial adenopathy; in **pertussis** and other **spasmodic coughs;** in **laryngismus stridulus;** in **palpitations** associated or not with hypertrophy of the heart, and in **convulsions.**

[The foregoing symptomatic indications are not approved by the writer, being merely offshoots of the prevailing empirical (and therefore unscientific) methods in the use of remedies. It is not to "allay spasm," to "reduce the heart's action," or to "reduce fever" that aconite should be given, but only where it may aid the curative process or offset complications as shown below. C. E. de M. S.]

The physiological effects enumerated afford sufficient ground for its value in the reduction of all the phenomena attending the **fever:** high temperature, dry skin, hard and frequent pulse, etc.

The tincture is preferable here, as it is in all other disorders. The best effects are produced by means of small doses. One minim is first given, then another minim in one-half hour. After that, 1½ minims are given every half-hour until the febrile symptoms are reduced or until physiological symptoms of the drug appear. Aconite should always be greatly diluted.

Its antipyretic power being less than that of certain newer remedies (coal-tar antipyretics), however, the latter generally (though very much less than formerly) find more favor where a marked reduction of temperature is desired, unless the additional indications for the use of aconite, such as an overactive heart, frequent pulse, or dry skin, be strongly marked. Its action in favoring perspiration may be enhanced by combination with other diaphoretics, such as the alkalies or pilocarpine.

Aconite is used in the fever attending the incipient stage of **catarrhal disorders**. It may be used as an antipyretic in continued fevers and infectious diseases,—**variola, scarlatina, erysipelas**, etc.,—but large doses are usually required, involving correspondingly great danger. It is better used in moderate doses for general sedative and diaphoretic effects in less severe infectious fevers, such as **measles**, mild scarlatina, **rubella**, and in the group of "**ephemeral**" **fevers**. According to Tison, aconitine reduces the pain and shortens the duration of **erysipelas**; he used aconitine nitrate in doses of $\frac{1}{640}$ grain every two hours, not exceeding 10 such doses daily.

In the **reflex fever** which sometimes follows the use of the catheter it has been found very efficient by several observers.

[In all these conditions the use of aconite should not aim to reduce the fever, but to aid in the destruction of the pathogenic substances, toxins, toxic wastes of which the febrile process is attempting to rid the blood. This is done with the aid of the small doses indicated above. By producing a slight depression of the sympathetic center, these small doses cause a correspondingly slight relaxation of all arterioles; they increase the volume of blood admitted into the capillaries, and, these minute vessels being the seat of the active febrile process, they hasten its activity and favor thereby the early destruction of the pathogenic substances.

Clinical experience has emphasized the fact that small doses are alone beneficial. From the explanation I have given of the effects of large doses, it is obvious that, by causing excessive dilatation of the arterioles, they can arrest the febrile process and place the patient at the mercy of the germs and their toxins. Large doses of aconite I deem worse than useless. C. E. DE M. S.]

In acute disorders of the nose, throat, and lungs the sedative effects exerted by aconite upon respiration through its influence upon the respiratory center are added to the qualities previously enumerated. Hence its value in **acute coryza, pharyngitis, tonsillitis, tracheitis, bronchitis, pleurisy**, and **pneumonia**. Dujardin-Beaumetz uses aconitine when the lungs are congested, and especially in **influenza**. In all of these, 2 drops of the tincture every hour should be administered until the physiological effects—tingling and numbness of the lips and tongue—are experienced, when the remedy should be given less frequently. After the initial stage of the affections enumerated, aconite should be discontinued, especially in **pneumonia**, in which affection its administration is positively harmful as soon as the asthenic stage begins. Aconite has been used in **hemoptysis** and **epistaxis** to lower the blood-pressure and favor cessation of the hemorrhage. In

the chronic disorders of the respiratory passages—including phthisis—it is more hurtful than beneficial.

In children aconite has proven useful in **coryza, tonsillitis, spasmodic croup, asthma, whooping-cough,** etc.

[The principles outlined in the foregoing commentary are quite applicable. The physiological effects need not be reached, however, to obtain salutary effects. It is in the early treatment of catarrhal disorders due to cold and exposure that aconite is most beneficial. The patient should, however, remain at home owing to the diaphoretic action of the remedy, which exposes to additional cold if exposed outdoors. C. E. DE M. S.]

Aconite has been employed in all forms of **rheumatism,** as well as in **gout,** to relieve pain and reduce congestion. It is especially indicated when the skin is dry. It is believed to have particular value in the acute rheumatic pains due to exposure. In chronic rheumatism it may be used in the form of a 2 per cent. ointment of aconitine. Hutchinson has found tincture of aconite beneficial in **rheumatic iritis.** He gives 5 minims three times a day, in conjunction with potassium iodide and the alkalies.

Meningitis, pericarditis, and **peritonitis** are mentioned concurrently owing to the fact that their early manifestations are equally influenced by aconite. In **peritonitis** especially, its effect as an anodyne tends to prevent vomiting: an important feature. In pericarditis it increases the chances of recovery by reducing the number of pulsations, thus prolonging the resting periods between beats. It should, however, be used with caution in these conditions, in view of its somewhat variable general depressant action.

[It happens that the four diseases referred to in the above two paragraphs: rheumatism, meningitis, pericarditis, and peritonitis, are all ascribed by the writer to excessive activity of the protective resources of the body, with autolysis of the tissue involved in these conditions as the direct pathological process. An important feature of the latter is the marked rise of blood-pressure which an excess of antitoxic bodies produces; it is this feature that aconite counteracts. By depressing the sympathetic center it causes relaxation of all arterioles, and thus lowers the blood-pressure. It is doubtful, however, whether it enhances at all the curative process. C. E. DE M. S.]

The sedative effect of aconite upon the sensory nerves and nerve-endings has led to its frequent use, internally or locally, in **neuralgia** and **neuritis.** Certain authors consider it specially effective in **neuralgia** of the trifacial nerve. In neuralgia of the intermittent type, a combination of aconite with quinine will often be found serviceable. In the form of neuralgia characterized by exacerbations during damp weather aconite is sometimes effective in small doses frequently repeated. If the painful spot does not cover much surface, application of the tincture over it with a camel's hair pencil contributes markedly to hasten the relief. The drug may also be applied as a liniment or by inunction (see Modes of Administration). The pain of **neuritis** resulting from exposure to cold is sometimes favorably influenced by aconite. In pain due to disturbances of the central nervous structures, however, the drug has not been found of great value.

[Neuralgia also includes an abnormal rise of the blood-pressure in its pathogenesis, according to the writer's interpretation of this disease (see "Internal Secretions," p. 1529), the pain being the result of congestion of the nervous elements of the affected area owing mainly to local vascular disorders. Aconite, by lowering the general vascular tension, relieves the pressure in the neuralgic area and the pain due to it. C. E. DE M. S.]

By lowering arterial tension and diminishing the number of heart-beats it may be of marked advantage in functional **cardiac disorders,** but when organic lesions are present it had better not be used. It is not infrequently employed in uncomplicated **hypertrophy, in nervous palpitation,** and in the **tobacco-heart,** to antagonize exaggerated action, but its effects should be closely watched lest incipient degeneration be present. The dose generally used is from 2 to 5 minims of the tincture three times daily.

[One cannot be too careful in using aconite in cardiac disorders, though the praise accorded it by various authors as the ideal remedy for the diminution of the blood-pressure when the heart is exposed to excessive resistance is also warranted by the interpretation of its physiological action I have submitted in the foregoing commentaries. C. E. DE M. S.]

> Toward no drug in the entire pharmacopeia is idiosyncrasy so often manifested. Numerous cases are recorded of dangerous syncope, and even death having resulted from small medicinal doses of aconite .(Ferrand, Leigh, Woodbury). Ferrand, indeed, emphatically condemns it as a dangerous drug the use of which should be confined to the laboratory. While few would go the full length of Ferrand's condemnation, great caution is undoubtedly necessary in its employment, owing to the unexpected susceptibility which is often manifested toward its action. We may well pause before undertaking a more extensive use of this drug in cardiac therapy. Arthur R. Elliott (N. Y. Med. Jour., Jan. 9, 1904).

[Since the 1905 U. S. P. has reduced the strength of the tincture, however, the dangers to which Elliott refers have been greatly reduced. C. E. DE M. S.]

A 2 per cent. ointment of the alkaloid aconitine has sometimes been applied to relieve pain and itching in affections such as **herpes zoster, eczema, pruritus,** etc.

> As suggested by Dr. G. W. Roberts, a solution of aconite in water is very efficient in stubborn **pruritus.** One dram (4 Gm.) of the tincture in 8 ounces (250 Gm.) of water or twice this strength may be used to "bathe" the itching area, using a soft cloth or sponge. H. T. Webster (Ellingwood's Therapeutist, Sept. 15, 1909).

Dysmenorrhea due to congestion of the pelvic organs, **metrorrhagia,** and **amenorrhea** resulting from exposure to cold have all been markedly benefited by aconite. In the **vomiting of pregnancy** aconite in moderately large doses is often found to give relief, owing to its sedative effect upon the nervous structures involved in the reflex act.

Aconite has been used with benefit in **acute gonorrhea,** 1 minim of the tincture being given every hour (Ringer). It is also advantageous as an anodyne in **epididymitis.**

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AND
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Philadelphia.

ACROCYANOSIS. See VASCULAR SYSTEM, DISORDERS OF, under ACROPARESTHESIA.

ACROMEGALY: PIERRE MARIE'S DISEASE. — **DEFINITION.** — Acromegaly is a general syndrome due, in almost every instance, to tumor of the hypophysis, characterized by progressive enlargement of the osseous and other supporting tissues, and primarily and chiefly noticeable in the extremities.

[Pierre Marie (Revue de Médecine, 1886, p. 297; Nouv. Iconog. de la Salpêtrière, 1888; Progrès Médical, March, 1889; Brain, 1889;

Revue de Médecine, Jan., 1890; "Leçons de clinique médicale," Paris, 1896; Bull. et Mémoires de la Soc. Méd. des Hôpitaux de Paris, 1896), in 1885, wrote a monograph entitled: *"De l'acromégalie, hypertrophie singulière, non-congénitale, des extrémités supérieures, inférieures et céphalique."* In it he described the deformities which he had observed in 2 cases from Charcot's service at the Salpêtrière, mentioning the increased bulk of the hands, feet, and of certain facial bones (nasal, malar, and inferior maxillary), the spinal curvature, as well as a "family likeness" which suggested that the two cases were suffering from the same disease. This affection he regarded as a special morbid entity. He concluded his paper with the words: "There exists an affection especially characterized by hypertrophy of the feet, hands, and face, which we propose to name *acromegaly* (from ἄχρον, extremity; μέγας, large), *i.e.,* hypertrophy of the extremities; acromegaly is entirely distinct from myxedema, from Paget's disease, and from the leontiasis ossea of Virchow."

This contribution did not appear until April, 1886, in the "Revue de Médecine." A new dystrophy had thus been added to the nosologic gamut. It presented manifestations so peculiar that it could not only be differentiated from similar affections, but even recognized from a distance. Verstraeten (Revue de Médecine, No. 5, 1889) and de Souza-Leite ("De l'Acromégalie, Maladie de Pierre Marie," Thèse de Paris, 1890) very rightly, therefore, designated acromegaly *"Pierre Marie's disease."*

It is but fair to recall, however, that the deformities had been mentioned in a number of earlier communications, of which a list may be found in a paper by Patry (Thèse de Paris, 1907). The most striking observations were those of Saucerotte (Mélanges de Chirurgie, part i, p. 407, 1801, and Mém. de l'Acad. de Chir., 1772), of Alibert (Précis théorique et pratique des maladies de la peau, t. iii, p. 317, Paris, 1882), of H. Henrot (Notes de clin. méd. Reims, 1877 and 1882); the last of these dealt with a case of acromegaly studied and examined *post mortem* by one of the writers of this paper. These had remained isolated observations, however, and ranked as mere curiosities. Once accurately known and described, the affection can be recognized in every case; for this reason communications bearing on it have been rapidly accumulating. In France, Pierre Marie (Nouv. Icon. de la Salpêtr., 1888; Progrès Méd., March, 1889; Brain, 1889; Rev. de Méd., Jan., 1890) completed the data presented in his first monograph. Guinon (Gaz. des Hôp., No. 128, Nov. 9, 1889), Rauzier (Nouv. Montpellier Méd., p. 623, 1893), and Blocq (Gaz. hebdom. de Méd. et de Chir., 1894) reviewed thoroughly, giving numerous references, the earlier communications on the subject, as did also Souza-Leite and Duchesneau (Thèse de Lyons, 1901) in their theses. The latter laid the foundations for pathological studies of the dystrophy. In other countries, the investigations bearing on this affection were no less plentiful, as shown in the tables published by Collins (Jour. of Nerv. and Ment. Dis., Nos. 1 and 2, page 139) in 1893. In view of their great number, we can mention but a small proportion of the authors on this subject. In America: Adler, Saundby, Duller, Harris, Osborne, Graham, Hary, Packard, Dercum, Berkley, and Moncorvo Diana, Woods Hutchinson. In England: Hadden, Silcock, Waldo, Paget, Bury, Kantack, Waddel, Campbell, Boyce, and Beadles Whyte. In Belgium: Verstraeten. In Germany: Virchow, Erb, Schültze, Ewald Gerhardt, Moebius, Mosler, Lethaun, Boeltz, Bier, Pel, and Fraentzel. In Italy: Caselli, Sacchi, Grocco, Bignani, Tanzi, Denti, Orsi, Bruzzi, Massalongo, Lombroso. In Russia: Burchard, Shaporonikow, Gorzatchew, Gazkienwiczi, Stembo.

This lengthy, though very incomplete list bears witness to the interest awakened in medical circles by the study of acromegaly since the year 1886.

In a second and no less fruitful period, investigators sought to determine the relations between acromegaly and gigantism [Pierre Marie (Leçons de clin. méd., Paris, 1896; Bull. et mém. de la Soc. Méd. des Hôp. de Paris, 1896), Brissaud et H. Meige (Jour. de méd. et de chir. prat., Jan. 25, 1895; Nouv. icon. de la Salpêtr., 1897), Meige (Congrès de neurol. de Grenoble, 1902, and Arch. gén. de méd., p. 410, Oct., 1902), Brissaud (Bull. de la Soc. Méd. des Hôp. de Paris, May 15, 1896), Launois et P. Roy (Bull de la Soc. Méd. des Hôp. de Paris, May 8, 1903; Nouv. icon. de la Salpêtr., 1902; Revue neurologique, 1903; "Etudes

biologiques sur les géants," Paris, 1904), Pierre Roy (Thèse de Paris, 1903), Woods Hutchinson (N. Y. Med. Jour., vol. lxxii, Nos. 3 and 4, July, 1900), Cunningham (Trans. of the Royal Irish Acad., vol. xxix, p. 553, 1891), Dana (Jour. of Nerv. and Ment. Dis., vol. xviii, 1893), Tamburini (Centralbl. f. Nervenheilk., B. vii, p. 625, 1894), Taruffi (Caso della macrosomia, Annali univ. di med., p. 247, 1879), Massalongo (Riforma med., p. 157, 1892)], to ascertain the nature of certain manifestations accompanying the deformities, such as ocular disorders [Schültze (Berlin klin. Woch., No. 38, 1889), Ruttle (Brit. Med. Jour., p. 697, Mar. 28, 1901), Pinel-Maisonneuve (Soc. franc. d'ophthalmol., May, 1891), Bernhardt (Beiträge zur Symptomatol. u. Diagn. der Hirngeschwülste, Berlin, 1881)], glycosuria [Loeb (Deutsch. Arch. f. klin. Med., B. xxxiv, p. 449, 1884, and Hypophysis cerebri und Diabetes mell., Centralbl. f. inner. Med., 1898), Hansemann (Ueber Akromegalie, Berlin. klin. Woch., p. 417, 1897), Hinsdale ("Acromegaly," p. 20, Detroit, 1898), Finzi (Boll. della Soc. Med. di Bologna, No. 4, 1894), Strümpell (Deutsch. Zeitschr. f. Nervenheilk., 1897), P. E. Launois and P. Roy (Arch. gen de méd., 1903, and Bull. de la Soc. de Biol., 1903)], the cerebral manifestations, and psychic disturbances [Soca (Sur un cas de sommeil par tumeur de l'hypophyse)]. They were thus led on to study the relations between various disturbances and hypophyseal tumor formation [Woods Hutchinson, Modena (Rivista speriment. di freniatria, 1903), Caselli (Rivista di freniatria, Feb., 1900, and Reggio-Emilia, 1900: Studi anat. e speriment. sulla fisiopatologia della gland. pituit.), Launois and Roy (Autopsie d'un géant diabétique et acromégalique, Nouv. icon. de la Salpêtr., 1903), Klaus and van der Stricht (Bull. de la Soc. de Méd. de Gand, 1893), Fritsch and Klebs ("Ein Beitrag zur Pathol. des Riesenwuchses," Leipzig, 1884)], and to emphasize the idea of a distinct and characteristic group of symptoms,—the *hypophyseal syndrome*,—the existence of which was soon confirmed when the new means of exploring the cranium afforded by Roentgen's discovery was brought into use [Béclère (Bull. de la Soc. Méd. des Hôp. de Paris, Dec. 5, 1902; Presse méd., Dec. 9, 1903), Giordani (Thèse de Paris, 1906), von Rutkeroski (Charité, Annalen, 1904), Schüller ("Die Schadelbasis im Röntgenbild," Hamburger Abl., 1905)].

In 1901, Fröhlich (Wien. klin. Rundsch., 1901) pointed out the symptomatic value of the adipose tendency which sometimes accompanies the development of pituitary tumors; the subsequent observations of Erdheim (Ziegl. Beitr., Bd. xxxiii, 1903), of Boyce and Beadles (Jour. of Pathol. and Bacteriol., pp. 223 and 359, 1893), of von Hippel (Virchow's Archiv, Bd. cxxvi, p. 124), Mohr (Schmidt's Jahrb., Bd. xxx), Gloser (Virchow's Archiv, Bd. cxxii, p. 389, 1890), and Pechkranz (Neurol. Centralbl., Bd. xviii, p. 202, 1899) added precision to our views on this point. Indeed, the present tendency is to divide into two groups the dystrophic manifestations of the hypophyseal syndrome, some being referred, on the one hand, to the *true acromegalic type of Pierre Marie*, and others to the *lipomatous type of Fröhlich*.

The third, or surgical, period in the history of acromegaly [Schlosser (Wien. klin. Woch., 1906, and May 21 and 23, 1907), von Eiselberg (Centralbl. f. Chir., Aug. 29, 1908), Hochnegg (*ibid.*, p. 72, and Arch. f. klin. Chir., Sept. 2, 1908)] is of recent advent (1908). With both great boldness and assurance, operators have advanced to the attack of the pituitary tumor itself, witnessed, after its removal, regression of the characteristic deformities, and brought out most cogent papers in favor of the hypophyseal theory concerning the dystrophy. LAUNOIS AND CESBRON.]

SYMPTOMATOLOGY.—The most prominent characteristic of the "acromegalic dystrophy" is, as we have stated, a progressive enlargement of the extremities. Although the deformities are particularly noticeable in naturally prominent portions of the body, they also involve other regions, such as the skull, face, spinal column, and thorax, and are very marked in these regions as well.

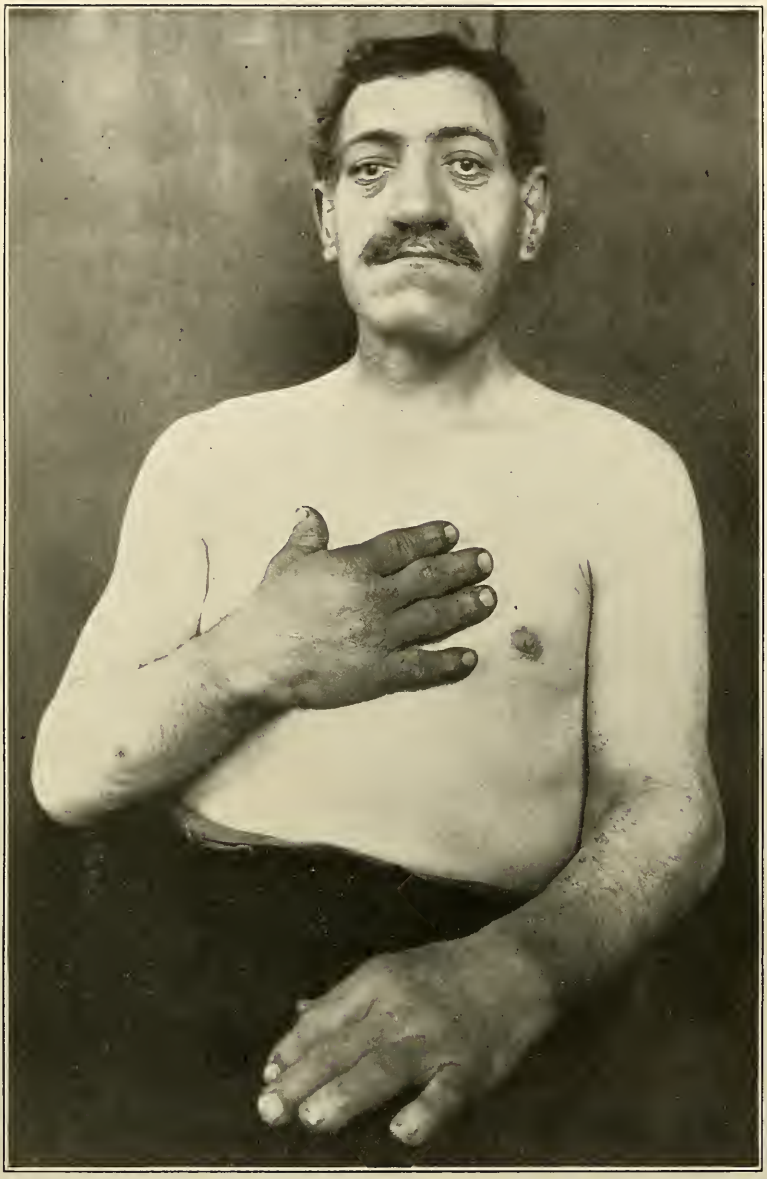
An outline of the general appearance of the acromegalic patient—that odd, ungainly, and unharmonious creature—

may prove profitable before the disease is studied in detail. His enormous, clumsy hands seem all the more massive from the fact that the forearms have retained their normal proportions. They present a "stuffed" appearance, and terminate in thickened, sausage-like fingers. His broadened feet are mere paws, with toes of exaggerated size. The face is long, the forehead narrow and retreating, and the supraorbital arches enlarged; the eyes often project forward from between the thickened eyelids; the nose stretches out laterally its fleshy alæ; the lips are enormous, especially the lower, which is everted; the lower jaw is strongly prognathic; the tongue, unusually large, frequently protrudes from the mouth. This repulsive and beast-like head, bounded laterally by ears of monumental size, is bent forward and set deeply between the shoulders. Though of average stature, or above the average, the subject appears partially collapsed; the curvature of his back and the thoracic deformity contribute to his humiliation, which is further accentuated by his torpid and melancholy demeanor. From a distance his appearance is so striking that the diagnosis can be made without detailed inspection. When the deformities are fully developed, all acromegalics bear a strong resemblance, and the adage, *"ab uno disce omnes,"* is here truly applicable.

The increased bulk of the *hands* is often the first change to attract attention. The hands become broader and thicker without augmenting in length. The hypertrophy involves all the component tissues of the part,—bones, muscles, subcutaneous cellular and fatty tissues, and skin. The latter is hard, firm, free of edema, and somewhat darkened in color. The interphalangeal folds, abnormally developed, extend between what may be called wads of flesh,—the "main capitonnée." The thenar and hypothenar eminences are greatly overdeveloped, and the linear grooves of the palm are transformed into deep gutters. The fingers are somewhat flattened from before backward, and are of equal thickness distally and proximally. The thumb measures up to 12 cm. in circumference (Lombroso), the index finger 9 cm., and the medius 10 cm. The nails remain relatively small. They become flattened, turn up at the edges, and show longitudinal striations. In exceptional cases a club-shaped deformity of the fingers, or the presence of nodosities at the interphalangeal joints, has been noted. Notwithstanding the unusual proportions of the acromegalic hand, its functions are generally preserved, complete flexion becoming impossible, however, in cases where the palm is markedly thickened. De Souza-Leite observed the "dead finger" phenomenon twice in 38 cases.

In contradistinction to this massive, voluminous, or *"transverse" type,* Pierre Marie has described a second variety of deformity involving the hands. In this type they again undergo a general increase in size, but there is added a growth in length which is about proportionate to that in breadth. Being longer, the hands thus appear lighter and less clumsy than in the massive form, where the overgrowth is almost solely transverse. This *"longitudinal" type* is seen more particularly in subjects in whom the dystrophy developed at a relatively early period. We have met with it in our infantile acromegalic giants.

These deformities of the hand generally stop at the wrist, at least during the earlier stages. Later on, the hypertrophy becomes generalized, the other



Acromegaly. (*P. E. Launois.*)

Acromegalic Profile. (*P. E. Launois.*)

segments of the upper extremity—forearm and arm—being also involved.

The *feet*, like the hands, become broader and thicker, without greatly increasing in length. They present the same fleshy pads, surrounded by deep grooves. The skin is darker, but is of similar consistency. The toes, especially the great toe, reach altogether remarkable dimensions, and the nails are affected much as in the upper extremity. According to Verstraeten, the heels are always enlarged. The hypertrophic enlargement generally terminates above the leg. The knee, if early involved, is enlarged but slightly, and the foot always contrasts, by its exaggerated bulk, with the rest of the limb.

The acromegalic *facies*, besides the characteristics already noted, includes a striking prominence of the supraorbital ridges, which project to an extent corresponding to the degree of enlargement of the frontal sinuses. The eyes are lacking in expression, and appear relatively small in comparison with the capaciousness of the orbits, notwithstanding the exophthalmos occasionally observed. The eyelids are thickened either *in toto* or merely in the region of the tarsal cartilages. The temporal fossæ becoming deeper, the malar prominences appear to stand out more strongly. The nose undergoes general enlargement, and is distinctly broadened and flattened. Its alæ are heaviest inferiorly, and the septum is doubled in thickness. The lips are enlarged, particularly the lower, which is also everted. The mouth, often half open, reveals a tongue of enormous bulk. The movements of the tongue are poorly executed; the organ interferes with mastication and articulation, is frequently injured by the teeth, and sometimes shows fissures at its borders. The roof of the mouth, soft palate, faucial pillars, tonsils, uvula, and larynx all exhibit hypertrophic changes. In female subjects, the thyroid cartilage, in its hypertrophied state, recalls the "Adam's apple" normally seen in the male. Laryngoscopic examination reveals both elongation and thickening of the vocal cords. These various changes in the organ of phonation impart to the voice a distinctive deep and at the same time metallic quality.

While the alterations in the superior maxilla are apparently not pronounced, those involving the lower jaw are sometimes extremely marked. The chin, large and massive, projects downward and forward, forming an obtuse angle with the rami of the jaw-bone. The lower teeth, which Henrot has found to be hypertrophied, are spread apart, and, owing to their forward projection, can no longer be opposed to the upper dental arch.

The profile is most characteristic, and bears witness to the extraordinary degree of prognathism sometimes attained. The description of the acromegalic facies would not be complete without a mention of the broadened ears, with their lobules of exaggerated size.

The facial skin is dry, brownish yellow in color, and often presents warty excrescences. The hairs covering the head are individually thickened, and, taken collectively, apparently exhibit a heavier growth. The eyelashes and other short hairy appendages are also coarse and stiff.

The *bones* of the cranium proper show modifications similar to those in the facial bones. These changes will be described later, when the results obtained by radiographic examination are discussed.

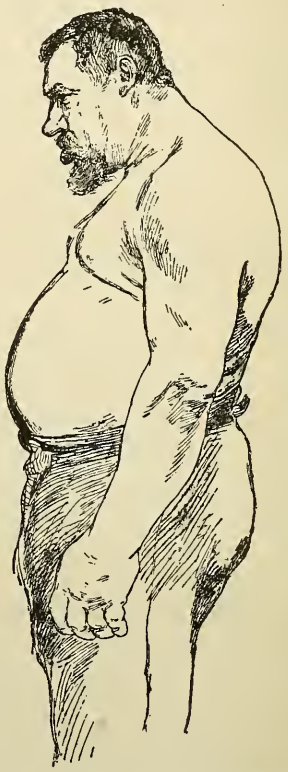
In the spinal region, the vertebræ, taken as a whole, show increased volume. As a result, changes in the spinal curves are brought about, consisting, more specifically, of a cervicodorsal kyphosis, with or without lumbar lordosis and scoliosis.

The thorax becomes more capacious and undergoes alterations in shape. It becomes prominent anteriorly. Though its anteroposterior diameter is increased,

Acromegalic macroglossia. (*P. E. Launois.*)

it is flattened laterally. The broadened sternum tends especially to spread out above, and develops transverse ridges. The clavicles become thickened and their curves exaggerated. The ribs come mutually into contact, or even overlap, and the costal cartilages become ossified. The lower costal arches slant downward, sometimes so markedly as to reach the crest of the ilium when the subject is in the sitting posture. The scapulæ are thickened, and their acromial and coracoid processes stand out in bold relief beneath the skin.

These deformities interfere in some degree with the thoracic excursions, sufficiently so, indeed, to bring about, among acromegalic subjects, a modification in the type of breathing, which becomes permanently abdominal. When they are all present in the same patient and are very pronounced, a double hump in the back may be pronounced, recalling the classic conformation of the Ital-



Cervicodorsal kyphosis in a case of acromegaly. (*Pierre Marie*)

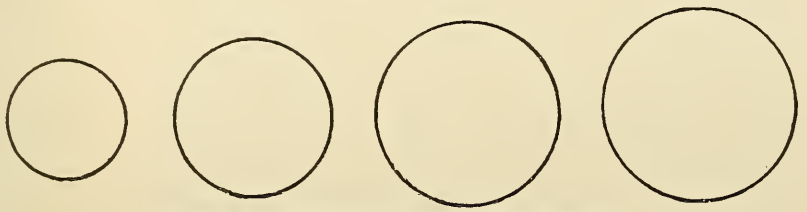
ian Punchinello, whom Pierre Marie considers the ancestor of acromegalics.

The dystrophy makes its first appearance at the distal ends of the extremities. The patient's attention is often attracted to the condition by the constantly increasing tightness of his gloves and footwear. In some instances the family or neighbors notice changes taking place in the facies. Once established, the affection progresses steadily and more or less rapidly. If the patient

Acromegaly in the Aged—Strabismus. (*P. E. Launois.*)

be a woman, she becomes aware of the progressively larger size of thimble she requires in her sewing. The male patient, on the other hand, is struck by the increasing diameter of his headgear.

From the distal portions, the changes proceed to the proximal segments of the limbs, which, by their hypertrophy, may assume a markedly athletic aspect. Muscular power, however, almost always shows a gradual decrease; notwithstanding their bulk, the contractile power of the muscles does not bear the normal ratio to their size. A certain degree of muscular atrophy has occasionally been noted; in a case studied by Duchesneau (Thèse de Lyon, 1901) it was so pronounced as to lead this observer to suggest the advisability of differentiating an *amyotrophic form* of the disease. The muscles show no noteworthy electrical disturbances; their excitability is diminished according to Erb, exaggerated according to Verstraeten. The patellar reflexes are either normal, diminished, or lost; they are never exaggerated.



Series of thimbles used by an acromegalic woman.

In certain *joints,* such as the knee, wrist, and elbow, there have been observed enlargement and painful crackling, recalling somewhat the phenomena noted in mild arthropathies.

The *circulatory system* presents an interesting group of alterations. Varicose veins are said to be frequent, and the heart is often hypertrophied.

[In 1895 Huchard pointed out the existence of more or less marked cardiovascular disturbances. His pupil, J. B. Fournier (Thèse de Paris, 1896), having collected 25 cases, including 12 with autopsy, was led to distinguish two varieties of cardiac hypertrophy, the one, slight and without degeneration of the muscular fibers; the other, accompanied by sclerosis and atrophy of the contractile elements. LAUNOIS AND CESBRON.]

Symptomatically these changes in the cardiac tissues find their expression in palpitations, arrhythmia, and dyspnea, and may result finally in asystole. Syncopal attacks are said to be not uncommon. Spinal deformities, when marked, may result in dilatation of the right heart.

Hypertrophy of the *lymphatic vessels and glands* has also been reported.

Sensation, on the whole, does not appear to be affected. Unusual sensitiveness to cold is, however, present to a certain extent.

The various deformities that we have described arise and progress, as a rule, without giving rise to pain. In some instances, however, their development is accompanied by more or less severe painful crises, sometimes referred to the viscera, at other times to the limbs. While sometimes taking the form of a simple myalgia, they may also develop into severe neuralgia, and are then aggravated by exposure to cold and dampness. This *painful form* of the disease (Sainton and Staté, Revue Neurologique, p. 30, 1900, and Thèse de Paris, 1900) may also assume the *rheumatoid type* when it becomes localized in a certain group of joints.

THE HYPOPHYSEAL SYNDROME.—Until recent years the natural history of acromegaly would have been covered by a description such as the above. The advances since made, however, both along clinical lines and in the pathology of the disease, owing to the use of the X-rays and to improved histological technique, have brought about modifications of our earlier ideas. Previously considered an individual affection, to which the name "Pierre Marie's disease" had properly been applied, acromegaly was found to be, in reality, only the most peculiar and striking component of the syndrome resulting from tumors of the hypophysis, and it is because it has drawn our attention to the hypophysis that the syndrome due to hypophyseal growths has brought forth such a wealth of literature as to make it at present, perhaps, the most abundantly discussed of the syndrome caused by brain tumors.

We consider acromegaly to be an integral part of the hypophyseal syndrome, and, indeed, with the exception of certain rare cases acromegaly unaccompanied by tumor of the hypophysis does not occur, while, on the other hand, the close relationship of the disease to such tumors seems established.

[The rare cases referred to are critically reviewed in the important papers of Woods Hutchinson (N. Y. Med. Jour., Nos. 3 and 4, July, 1900), and of Modena (Rivista sperimentale di freniatria, Fasc. iii and iv, 1903), and of which only one, that of Bonardi (Riforma medica, ii, 1893), is of value as evidence. LAUNOIS AND CESBRON.]

The affection generally makes its appearance long before the other components of the syndrome, which may be interpreted as disturbances due to compression; on the other hand, in no case has a tumor in the region of the hypophysis been known to produce acromegaly unless developed from the hypophysis itself. Acromegaly almost certainly implies the existence of a tumor of the hypophysis. The converse is, however, not always true, every tumor of the hypophysis not necessarily resulting in acromegaly.

Clinically, tumors of the pituitary, the frequency, nature and characteristics of which we shall mention later, betray their presence by an aggregate of signs and symptoms included under the term "hypophyseal syndrome." We may divide these signs and symptoms, following the example of the obstetricians, into the three following groups: 1. Probable signs and symptoms of pituitary tumor. 2. Quasi-positive signs and symptoms. 3. Positive signs.

The first are those of *brain-tumor with special localization.* Through its increased size, the pituitary expands the bony fossa in which it is lodged and soon begins to project upward above it, indenting the lower surface of the cerebrum. It exerts more or less pressure on the neighboring structures, and causes a certain degree of increased intracranial tension.

The earliest symptom of it is *headache.* The pain tends to become localized anteriorly; these patients often complain of a sensation of heaviness "which impels them half unconsciously to rub their forehead and eyes, as one does ordinarily upon awakening" (Rayer). In certain cases, the pain is more definitely localized.

[In a patient under the observation of Bartels (Zeitschrift f. Augenh., xvi, pp. 407 and 530, 1906), it radiated even to the eyes, and was of great intensity. In other instances mild neuralgic states, as in the case reported by Infeld (Sitzungsb. des Vereins f. Psych. u. Neurol., Wien, 1902), may be present, or, again, severe involvement of the trigeminal may exist. In a

patient under the care of Benda (Berliner klin. Wochenschr., p. 167, 1897), the pain was so severe as to require removal of the Gasserian ganglion. The pain has likewise been known to extend into the occipital region (Bartels), and ever to predominate there. Pontoppidan (Hosp. Tid., 1897) reported the presence simultaneously

Young acromegalic woman. In lower right-hand corner, same patient at the age of 20, soon after onset of the affection. (*P. E. Launois.*)

of right-sided trigeminal neuralgia and bilateral occipital neuralgia. The effects of the trigeminal involvement are sometimes so severe as to cause lagophthalmia or neuroparalytic keratitis, as reported by Hirschl (Wiener klin. Wochenschr., No. 10, 1899) and Grünwald (Münch. med. Wochenschr., No. 22, 1895). LAUNOIS AND CESBRON.]

In some cases the progress of the disease is so nearly painless that the discovery *post mortem* of an almost complete flattening of the basal convolutions, whereas in life only trifling migraine had been recorded, becomes a matter of surprise.

Along with the headache should be mentioned *vertigo* and *vomiting* of cerebral type, which are among the usual signs of intracranial tumors.

With the symptoms are generally associated *melancholic tendencies, loss of memory,* and *mental and physical torpor.* Apathy sometimes reaches such a degree that the power of executing voluntary acts seems practically lost. It was very pronounced in the peculiar case described by Rayer: "During the

morning visit, when asked to rise, he promised to put on his clothes at once, yet at 5 o'clock in the afternoon, notwithstanding repeated requests by the nurse, he was still in bed. When obliged to relinquish his room in the daytime, he would leave only to sit motionless in an armchair or to slumber in an adjoining room. The positions he assumed were those of an exhausted, flaccid, and semiunconscious individual." Convulsive movements may also be observed, sometimes confined to the face, in other instances involving the limbs.

["Cardinal de Bousy," as related by R. Vieussens ("Novum vasorum corporis humani systema," Amsterdam, p. 245, 1705), "at the age of 62 years was subject to convulsive movements affecting particularly the muscles of the eyes, lips, and tongue. At the outset of the malady the attacks were of short duration and recurred only at long intervals; later they became so frequent and were accompanied by pains of such exceeding severity as to exert a marked deleterious effect on the mental faculties, and especially on the memory, of the cardinal, who complained, in addition, of a certain sensation as of movements taking place within his head. Several apoplectic attacks then occurred. One of these strokes was so violent that the patient was stricken with right-sided hemiplegia, which later gradually disappeared." The patient died a short time after; at the autopsy a large tumor of the hypophysis was found. LAUNOIS AND CESBRON.]

In establishing a diagnosis of brain tumor in general, and of tumor of the hypophysis in particular, no signs should be overlooked, and we must, therefore, not forget to mention as possible symptoms *cramps, contractures* (Berger, Zeitschr. f. klin. Med., liv; Stevens, British Med. Jour., April, 1903), and *trismus* (Koster, Hygieia, 1902). These may be related to the coexisting hydrocephalic condition, since they disappeared, in a patient of von Hippel (Virchow's Archiv, cxxvi, p. 124), upon the removal of cerebrospinal fluid through a nasal opening. The *tremor* observed by Stroebe and the *ataxia* of the lower extremities reported by Henneberg (Neurol. Centralbl., p. 518, 1902) are probably to be referred to some similar cause.

Peculiar *anomalies of taste* occasionally appear, consisting of strongly expressed desires on the part of some patients to eat most unusual articles of food.

Tinnitus aurium, peculiar in that it appears only on the side upon which the patient is lying, has been noted (Yamaguchi, Klin. Monatsschr. f. Augenheilkunde, 1903).

Pressure may be exerted upon the sinuses adjoining the hypophysis and cause disturbances in the venous circulation, as shown by *facial edema.*

Among the circulatory changes that may be produced is to be added to those already mentioned the somewhat paradoxical *acceleration of the pulse,* reported by Engel (Inaug. Dissert., Wien), Rosenhaupt (Berliner klin. Wochenschr., 1903), Infeld, and Bartels.

A no less singular manifestation is *lowering of the internal temperature,* which, in a patient of Bartels, remained for weeks at a time between 34° and 36° C. (93⅕° and 96⅘° F.) without the supervention of any sign of collapse.

[The same phenomenon has been witnessed by Petrina. In a case reported by Götzl and Erdheim (Zeitschr. f. Heilk., 1905) the temperature fluctuated for three weeks between 35° and 36° C., later falling to 33° C. (91⅖° F.). It would be rather difficult at this time to explain the origin of such disturbances; we shall merely point out their similarity to the phenomena observed in myxedema, in which disorder the temperature often fluctuates between 33° and 35° C., and sometimes even

falls below these figures. LAUNOIS AND CESBRON.]

Torpor and asthenia are, as we have stated, among the ordinary manifestations of acromegaly. Exaggeration of these symptoms, in the hypophyseal syndrome, may give the appearance of *"sleeping spells"* (Soca, Nouv. Iconog. de la Salpêtrière, No. 13, p. 101, 1900), similar to those sometimes accompanying cerebral tumors (Raymond, Oppenheim, Buens).

True psychoses occur with extraordinary frequency in cases of tumor of the hypophysis. Schüster ("Psychische Störungen bei Hirntumoren"), who has made a special study of the psychic disturbances observed in brain tumors, believes that they are met with in almost one-half of the cases of tumor of the hypophysis. This proportion will not seem surprising if we recall the fact that the first pathological observations on hypophyseal tumors were made in asylums for the insane (Rullier, Présentation à l'Académie royale de Médecine, Oct. 7, 1823). History affords a conspicuous example of this in the person of Cromwell's giant porter, a maniac with prophesying tendencies, whom it was found necessary to confine.

In the literature on the pathology of tumors of the hypophysis we often come across the words *"amaurotic insanity"* as a heading in clinical records. This accompaniment of these tumors, long overlooked, was but recently given due emphasis by Fröhlich, and particularly by Cestan and Halberstadt (Revue neurologique, p. 1180, 1903). The various forms of delirium, delusions of persecution, mystery, and the manic-depressive psychosis may be encountered. An interesting fact has been reported by Moutier ("Acromégalie: crises épileptiformes avec équivalents psychiques," Revue neurologique, Nov. 8, 1906) in the occurrence in an amblyopic acromegalic of rather frequent epileptiform seizures, due evidently to the cerebral tumor present. In the intervals between seizures he was subject to "absent periods," during which he would sometimes remain perfectly still, or else perform a large number of unreasoning acts of which he lost all remembrance after the attack had subsided.

[In France, Brunet (Thèse de Paris, 1899), Joffroy, Roubinowitch (Bulletin médical, 1908), and Barros (Thèse de Paris, 1908) have made special studies of the mental condition of acromegalics. LAUNOIS AND CESBRON.]

Polyuria and *glycosuria* are often encountered in cases of tumor of the hypophysis. That the presence of sugar was not more frequently reported by the earlier observers is due to the fact that they were not in the habit of examining the urine in their cases systematically. Loeb (Deutsch. Archiv f. klin. Med., p. 449, xxxiv, 1884; Centralbl. f. innere Med., 1898) was the first to point out the frequency of melituria in disease of the hypophysis. He explained it as being due to the pressure which may indirectly be exerted by tumors of this gland on the floor of the fourth ventricle and neighboring structures.

[According to Pierre Marie, glycosuria occurs in one-half the cases of acromegaly. Von Hansemann (Berliner klin. Wochenschr., p. 417, 1897) found it in but 12 of the 97 cases he collected, and Hinsdale ("Acromegaly," p. 20, Detroit, 1898) in but 14 out of 130. The figures of these last observers are not to be taken as standards, however, for very often the presence of glycosuria was not tested for. All the papers bearing on this question have been brought together in the communications of Loeb, Pineles (Jahr. der Wien. Krank., iv, 1897), Caselli (Rivista di freniatria,

February, 1900; "Studii anatomici e sperimentali sulla fisiopatologia della glandola pituitaria," Reggio-Emilia, 1900), Launois and Roy (Nouv. Iconog. de la Salpêtrière, 1903; Archives générales de Médecine and Bull. de la Soc. de Biol., 1903; Bull. de la Soc. Méd. des Hôp. de Paris, May 8, 1903; Nouv. Iconog. de la Salpêtrière, 1902; Revue neurologique, 1903; "Etudes biologiques sur les géants," Paris, 1904; Pierre Roy, "Contribution à l'étude du gigantisme," Thése de Paris, 1903). There is a tendency among certain authors, on the basis of the association of glycosuria with acromegaly, to distinguish a special syndrome, to which von Noorden ("Handbuch der Stoffwechselskrankheiten," vol. ii, p. 45, 1905) has given the name *"acromegalodiabetes."* LAUNOIS AND CESBRON.]

Glycosuria of hypophyseal causation, though more or less constantly present, may show wide variations in intensity. In a patient of Finzi (Boll. della Soc. Med. di Bologna, No. 4, 1894), for instance, the sugar, after having been present in large amounts, gradually disappeared completely from the urine. In February, 1888, Strümpell (Deutsch. Archiv f. Nervenheilkunde, 1897) noted a marked glycosuria in one of his cases. In May of the same year the sugar had disappeared. It reappeared in October, then did not return, even after the ingestion of a large quantity of carbohydrates. These variations are probably to be explained, in common with the ocular disorders we shall discuss later, by the variations that may occur in the size of the pituitary tumors. It is rather difficult at present to explain the mode of production of hypophyseal diabetes, and the various theories advanced regarding its pathogenesis have none of them received sufficient confirmation.

> Of the 176 cases of acromegaly reported so far, 35.5 per cent. included glycosuria as a symptom. Experiments to ascertain whether this was due to functional perversion of the pituitary, by injecting hypophyseal extract obtained from men and horses into dogs and rabbits. In dogs no uniform results were obtained, but in rabbits a glycosuria varying from a slight trace to 4.2 per cent. always occurred. Borchardt (Zeit. f. klin. Med., Bd. lxvi, S. 332, 1908).

Dallemagne (Archives de Médecine expérimentale, 1895), Pineles, and von Hansemann have found lesions of the pancreas at the autopsy. The first of these observers, in addition, noted the presence of small gliomatous formations in the region of the fourth ventricle.

According to Lorand (Journal médical de Bruxelles, 1903), the glycosuria results from disturbance in the internal secretion of the hypophysis, and is a component of one of the polyglandular syndromes, to learn the precise nature of which investigations are now being conducted.

Loeb believes it due to pressure exerted on the structures at the base of the brain, and, since, of all cerebral tumors, those developing from, or in the neighborhood of, the hypophysis are the most likely to cause glycosuria, he is of the opinion that a center regulating the metabolism of sugar exists in this region. The center discovered by Claude Bernard in the floor of the fourth ventricle would thus not be the only one of this kind; Schiff, indeed, appears to have found other such centers in the optic thalami, crura cerebri, and pons. Eckhardt produced glycosuria in rabbits by injuring the vermis of the cerebellum, and, returning to clinical and pathological records, we may recall that Lépine observed diabetes in a case of softening of the central gray nuclei, and Loeb and Naunyn in cases of cerebral hemorrhage.

According to the views of Sajous

("The Internal Secretions and the Principles of Medicine," vol. i, 1903; vol. ii, 1907; Gazette des Hôpitaux, Mar. 10, No. 29, 1907), who holds that a nervous center exists in the hypophysis, and that the several ductless glands are connected by a nervous pathway, a ready explanation is afforded. Diabetes of hypophyseal origin is the result of an irritation, a disturbance produced in the nervous center which the gland contains, in the same way that the nerve-path, in its bulbar course, is influenced by puncture of the fourth ventricle.

Whether we adopt the view of Loeb, involving pressure changes, or that of Sajous, relative to nervous irritation, however, the presence of an intermediary is further required for the production of glycosuria. According to some, this intermediary factor is the pancreas; in the opinion of Gilbert and his followers, it is the liver which, under these conditions, becomes functionally overactive; according to Sajous, it is the adrenals, to which he traced nerves from the pituitary, the adrenal secretion augmenting through increased oxidation the production of amylopsin, which, in turn, increases abnormally the conversion of the hepatic glycogen into sugar.

Rath, Oppenheim, Königshoffer, and Weil have reported polydipsia together with polyuria in the entire absence of glycosuria. Bouchard has observed peptonuria and Duchesneau phosphaturia.

Among the other disturbances of secretion, frequent and copious *sweating* should also be mentioned.

The anatomical and functional changes taking place in the *reproductive organs* in acromegalic cases were early recognized. The penis, which, as Erb correctly remarks, is also an "ἄχρον," sometimes, though not regularly, attains a greater size than normal. In the female, the clitoris may undergo corresponding hypertrophy, and the folds of skin forming its prepuce may become thickened.

This enlargement of the genital organs should by no means be taken to imply increased functional activity. Indeed, male patients usually experience a diminution of desire and potency, which may progress to complete loss of the function. In the female, the most important result is suppression of the menses, which occurs so early in the disease that in many cases it may be considered the initial event.

The primary increase in size in the genital organs soon gives way to a true atrophy. In certain cases of hypophyseal tumor which had not been accompanied by acromegaly, the penis was observed to have dwindled to the size of the little finger, the testicles to have become small and soft, and the pubic hair diminished in amount.

Pechkranz and Babinski were the first to report these changes. Roubinowitch published the interesting history of a patient, previously studied by Pierre Marie, who developed acromegaly after childbirth, and showed progressive atrophy of the organs of generation.

On the basis of published facts we may at present conclude that sexual atrophy can form part of the hypophyseal syndrome, but that it is not invariably a consequence of tumors of the hypophysis. Coming on in youth, these tumors may cause arrest of development of the genital organs; appearing later, they may cause retrogressive changes in them. The problem has not yet been solved, since it will be necessary to determine more precisely in what measure the hypophysis is capable of producing

genital atrophy. The experiments of Vassale, of Caselli, and of Sacchi seem to have demonstrated that removal of the gland in young animals is without effect on their sexual development, but these animals have never survived any length of time. Moreover, a certain number of cases have been known, including those of Schmidt-Rimplex, of Götzl and Erdheim, of Babinski (Revue Neurologique, vol. viii, p. 531, 1900), of Pechkranz, and of Bartels, in which the tumor causing genital atrophy did not involve the hypophysis.

In our description of the acromegalic dystrophy we stated that the hypertrophic changes witnessed were due to an abnormal development in the various connective tissues. This overgrowth may, however, be limited to certain parts of these tissues, and in particular to the panniculus adiposus. In 1901, Fröhlich (Wiener klin. Rundschau, 1901) drew attention to a special variety of adipose overgrowth occurring in cases of tumor of the hypophysis, and attaining considerable proportions. Erdheim (Ziegler's Beiträge, Bd. 33, 1903) confirmed the association of these two conditions, and a number of cases have recently been reported. The *accumulation of fat* under these circumstances is steady and more or less rapid. It may reach an enormous extent.

[A patient under the observation of Boyce and Beadles (Jour. of Pathol. and Bacteriol., pp. 223 and 359, 1893) exhibited a layer of fat several centimeters in thickness over the entire body. Adipose deposition occurs in the deeper parts as well as superficially, the great omentum, mesentery (von Hippel: Virchow's Archiv, cxxvi, p. 124), heart, and liver (Mohr: Schmidt's Jahrb., xxx) being invaded. A patient seen by Glaser (Virchow's Archiv, cxxii, p. 389, 1890) had enormous cheeks, which were livid and showed numerous dilated veins; Pechkranz's (Neurol. Centralbl., xviii, p. 202, 1899) case gave the impression of one suffering from anasarca, although pressure on the hands and feet failed to bring out the characteristic pitting of edema. Stewart (Boston Med. and Surg. Jour., No. 21, 1899) reported a similar observation. LAUNOIS AND CESBRON.]

With the adipose accumulations are often associated signs of increased intracranial tension, and at times, as we have remarked, mental disturbances.

We are not as yet in a position to explain the special involvement of the reserve tissues in this affection, but will have to limit ourselves to recalling the following interesting observation reported by Madelung (Langenbeck's Archiv, lxxiii, p. 1066): A girl 6 years of age, having been shot in the head, began to put on fat six months later. Her weight doubled in the space of three years and reached 42 kg. (92 pounds). Examination with the X-rays revealed the bullet in the region of the infundibulum.

Myxedema may form part of the hypophyseal syndrome. From the early observation of Norman Dalton (Lancet, No. 6, 1897) to that of Sainton and Rathery (Bull. de la Soc. Méd. des Hôp., May 8, 1908), a large number of cases have been reported which support the view that this combination may occur.

The simultaneous presence of *simple goiter* and of *Basedow's disease* [Lancereaux (Semaine médicale, 1902 and 1905)] has likewise been reported. Although the association of these disorders is a point in favor of the existence of a polyglandular syndrome, it would be rash at this time to attempt to define the latter precisely.

Ophthalmic Disorders.—The *quasi-positive signs* of the presence of a tumor of the hypophysis are found in a study of the ocular disorders, which result

Lipomatous Type of Fröhlich's Syndrome. (*P. E. Launois.*)

from the close anatomical relationship of the pituitary gland to the optic pathways. The visual disturbances long ago attracted and retained the attention of investigators. Among the earliest observations should be remembered those of Vieussens (1705), and of Rullier (1823). Ocular disturbances are also mentioned in the papers of Rayer and of Friedreich. Bernhardt has summarized them as follows: "Slow, progressive amblyopia, terminating in absolute blindness. Since the latter does not result from increased intracranial tension, but is generally due to pressure on the optic tracts, chiasm, and optic nerves, papillary edema is not generally present, primary atrophy taking place in most instances."

As for the events related more particularly to acromegaly, Pierre Marie at first recorded merely optic neuritis in mild cases, absolute blindness in advanced cases. Pinel-Maisonneuve in France, Schültze (Berl. klin. Wochenschr., No. 38, 1889) in Germany, and, later, Boltz (Deutsche med. Wochenschr., page 685, 1892), and Packard (Amer. Jour. of the Med. Sciences, p. 660, 1892), sought to emphasize the diagnostic value of bitemporal hemianopsia, *i.e.*, loss of vision in the lateral halves of the two visual fields, with preservation of central vision. Since these earlier investigations, numerous observations have been collected; the present tendency, based on these, is even to establish a distinction between tumors arising in the hypophysis itself and those developing simply in the hypophyseal neighborhood. The former are not, in general, accompanied by pronounced disturbances of vision until a rather advanced stage. The morbid change in the optic nerve, however, almost always progresses, and leads finally to complete amaurosis of one or both eyes.

The first sign afforded on systematic examination of the eyes is a diminution of visual acuity. But slightly marked at first, this generally undergoes gradual increase, absolute blindness being reached, in most instances, only after a period of ten or twelve years. Ordi-

Acromegaly with tumor of pituitary and goiter. (*P. E. Launois.*)

narily, one eye is more seriously affected than its fellow, and shows amaurosis at an earlier period.

[According to Uhthoff (Zusammenkunft der Ophthalm. Gesell., Heidelberg, Aug., 1907), unilateral amaurosis occurs in 33 per cent. of the cases. In other instances the amaurosis is bilateral (16 per cent.). The latter condition may sometimes appear at a very early stage of the disease, as in the cases reported by Leber (Archiv f. Psych., xxxi, p. 206) and Josefsohn ("Studier ofver akromegalie eck hypophysistumor," Stockholm, 1903). In Henneberg's case total amaurosis was present thirteen years before death occurred. LAUNOIS AND CESBRON.]

The condition sometimes runs a rapid course; it may disappear for a short time, then return and become definitely established. According to Oppenheim (Berliner klin. Wochenschr., No. 36, 1887, and No. 29, 1888), the histological structure of tumors of the hypophysis, which are frequently very vascular, bears a casual relation to this "oscillating vision." From the rupture of vessels with their walls in an embryonal, formative state, followed by more or less extensive hemorrhage, sudden blindness might result. Eisenlohr (Virchow's Archiv, lxviii, p. 461) reports the case of a man who, without having previously exhibited any pronounced disturbance, was suddenly seized with headache, vomiting, somnolence, and convulsive movements of the upper extremities. At the same time the pupils were dilated and fixed, and double amaurosis was present. The autopsy disclosed in the sella turcica a rounded tumor of the size of a cherry, the existence of which had not been suspected during life, and which had been the seat of an extensive hemorrhage. In like manner Bayley (Philadelphia Med. Jour., April, 1898) witnessed absolute blindness with partial oculomotor paralysis in a man of 50, who afterward showed a hemorrhagic focus in the hypophysis. With these observations may be grouped those of Bassoe (Jour. of Nervous and Mental Diseases, Sept. and Oct., 1903) and Yamaguchi. In the case of a young girl who suffered complete loss of vision in three weeks, Woolcombe (Brit. Med. Jour., June, 1896) discovered the presence of an exceedingly vascular psammoma.

Of still greater interest and importance are the alterations in the fields of vision which accompany tumors of the hypophysis, and occur with particularly remarkable frequency in acromegaly. From the standpoint of diagnosis they are of primary importance.

In 22 cases with autopsy in which changes in the visual fields had been recorded, the percentage of each form of hemianopsia was as follows: Bitemporal hemianopsia, 23 per cent.; unilateral temporal hemianopsia, 23 per cent.; homonymous hemianopsia, 9 per cent. Concentric reduction of the visual fields was recorded in 22 per cent. of the cases; an irregular contraction in 4 per cent.; in 9 per cent., but one quadrant was preserved; in 13 per cent. there was a central scotoma.

> Study of the eye symptoms in disease of the pituitary body and acromegaly based on 328 autopsies. Temporal hemianopsia is the most constant symptom; typical choked disk and slight papillitis each occurred in about 5 per cent. of the cases, simple atrophic pallor of the disks in 20 per cent., and central scotoma only in occasional cases. Paralysis of ocular muscles, generally affecting the oculomotor nerve, occurred in 10 per cent. of cases, and nystagmus in 6 per cent. W. Uhthoff (Lancet, Sept. 4, 1909).

These results will, at first sight, appear somewhat inconstant. This variability in the alterations of the visual fields is, however, to be accounted for by the fact that the visual tests were made at different stages of the affection in the various cases. It is evident that hemianopsia and scotoma are the two most important of these disturbances.

As Déjerine pointed out, the condition present is not, strictly speaking, a true hemianopsia, since its boundaries are practically never regular in outline, and the line marking off the blind from the unaffected portions of the visual field is never exactly vertical. True hemianopsia can exist only when the lesion, situated behind the chiasm, in-

volves the visual pathways in that part of their course which extends from the decussation to the cerebral cortex. At the chiasm itself the nerve-fibers have not yet undergone complete separation into definite bundles, and it is here that we must seek an anatomical explanation for the irregular hemianopsia which accompanies lesions of this portion of the optic pathway.

Moreover, the most varied combinations of the several ocular disturbances may occur. A central scotoma, for example, may be present at first, hemianopsia then appearing (Pontoppidan), or hemianopsia may precede and be later supplemented with marked contraction in the visual field (Strümpell). Hemianopsia and contraction are often found to coexist.

Central scotoma is of very frequent occurrence, but does not seem to possess any special value as an indication of the lesion present, since it has been observed in cases where the visual tracts appeared to be crushed by the tumor, and it is difficult to understand how, under such conditions, the maculopapillary fibers could alone be affected. Indeed, from the variations in the extent of involvement of the visual fields no conclusion can be reached with any degree of certainty as to the exact seat of the lesion. Changes in the visual fields are, however, almost constantly present; whenever examined for they have been found, and up to the present time Schönborn's case is, perhaps, the only one in which they were wanting. This observer, moreover, fails to state whether he studied the color-perception in his patient or not.

Among the changes in the eye-grounds in those suffering from tumors of the hypophysis, simple optic atrophy should receive first mention. Papillary edema, on the other hand, is of relatively rare occurrence.

[Bath, and later various other authors, among whom were Denti (Annali di Ottalmol., xxv, p. 615), Sternberg, Oppenheim, and Schmidt-Rimpler ("Die Erkrankungen der Augen in Zusammenhang mit anderen Erkrankungen," Vienna, 1905), found it to occur much less frequently than in other varieties of cerebral tumor. According to Bartels, 40 cases with autopsy yielded the following percentages: Simple atrophy, 50 per cent.; bilateral papillary edema, 15 per cent.; neuritis followed by atrophy, 15 per cent.; disks entirely normal, 20 per cent. LAUNOIS AND CESBRON.]

The uncommon occurrence of papillary stasis may be explained by the lesions resulting from direct compression of the optic-nerve bundles. We can readily believe, with Terrien, that an intimate union takes place very early between the nerve-fibers and their sheaths in the visual tracts, and that the adhesions formed between these structures make it difficult, or even impossible, for the cerebrospinal fluid to enter the papilla.

The pupillary reflexes in cases of hypophyseal tumor also afford an interesting study, in conjunction with the disturbances of vision already mentioned. In general, it may be said that they are always altered.

In a large number of cases simple amaurosis is observed, with pupillary immobility as a consequence. Thus in a case reported by Selke (Inaug. Dissert., Königsberg, 1891), the pupils did not react either to light or distance, though the patient could still distinguish light from darkness. In a case of unusual interest, Berger observed during a period of temporary amaurosis loss of the reaction to light, while the reaction to distance was preserved. The light reflex later reappeared. In other cases, where the patients are still able to recog-

nize objects, the reflexes persist, but are less active. Yamaguchi has even witnessed very slow response to light in an eye showing normal visual acuity.

Lastly, where hemianopsia exists, the hemiopic reaction may sometimes be observed. The well-known "hemianopsic pupillary reaction," discovered by Wernicke, implies inability on the part of a visual field to bring about pupillary action in response to light falling upon it. The pupillary fibers of the optic nerve pass into the anterior corpus quadrigeminum; from here a relay of fibers starts which places them in connection with the nucleus of the pupillary sphincter, located in the central gray matter of the aqueduct of Sylvius, in the anterior portion of the common oculomotor nucleus. When these pupillary fibers are destroyed, as in cases where the optic tract has been crushed or has disappeared completely, the blind half of the visual field can no longer cause pupillary action. This reaction, then, is characteristic of an interruption in the optic fibers at a point between the chiasm and the corpora quadrigemina. The hemianopsic reaction of Wernicke is thus an integral part and almost exclusively an attribute of the syndrome resulting from disease in the hypophyseal region.

We must admit that the presence of this reaction does not appear to have been shown very often. While Josefsohn observed it very clearly, Götzl and Erdheim, in a case of hemianopsia resulting from pituitary tumor, were unable to find it. This failure and the dearth of confirmatory observations should, perhaps, be attributed to the difficulties of technique which have to be overcome in order to demonstrate the existence of this singular pupillary disturbance, which is possessed of such great clinical value for the localization of brain lesions.

Radiographic Study of the Cranium.—As for the *positive signs* of the presence of a tumor of the hypophysis, they are afforded by X-ray examination of the cranium.

No sooner had Roentgen's discovery (1895) given us the power, as Giordani expressed it, "to make of the invisible an object" than the X-rays began to be utilized in the study of the skeletal dystrophies, and of acromegaly in particular. Marinesco brought out a comparative study of the bones of the hand in acromegaly of the massive and the giant types. The data collected by Gaston and G. Brouardel were sufficiently precise to admit of the following conclusion, *viz.*, that "radiographic studies of the acromegalic hand make it possible to trace the process of central bony reabsorption and the periosteal and cartilaginous proliferation which Pierre Marie and Marinesco observed in their histological studies."

To Béclère belongs the credit of having drawn from radiographic exploration the full measure of data to be derived therefrom in the study of the hypophyseal syndrome. His first attempts were fruitless because of an entirely abnormal thickening of the cranial bones, but his later researches, especially those carried out in cases sent him by us, were productive of more accurate results. He witnessed the simultaneous occurrence of three strongly characteristic changes: (*a*) *A very irregular thickening of the cranial parietes:* the outline of the skull, instead of being rounded, is polygonal; the external and internal tables, always separated by an abnormal space, alternately recede and come together, giving a moniliform appearance on cross-section. (*b*) *Exag-*

gerated height and depth of the frontal and maxillary sinuses. (*c*) A more or less marked *increase* in the vertical, and especially in the anteroposterior, *dimensions of the pituitary fossa,* which, markedly altered, in most instances presents the appearance of a cup. To these primary modifications must be added *exaggeration of the postlambdoidal prominence* (Papillaut, Launois, and Roy).

increase in the size of the fossa can be plainly appreciated at its posterior wall. Schuller believes that enlargement of the bony cavity is the rule, even where the tumor is of relatively small size, and of slow, regular growth. The bony parietes may, in certain cases, undergo pressure atrophy. In cases of rapidly growing tumor they likewise disappear, being invaded by the neoplastic tissue.

Erdheim has established still nicer

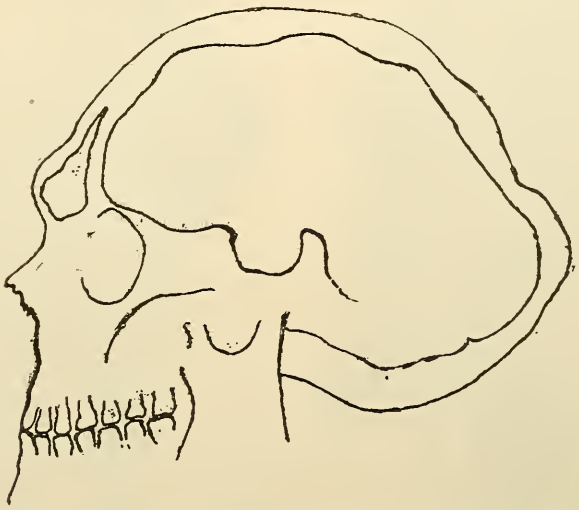


Diagram of the acromegalic skull, worked out by P. E. Launois and P. Roy, according to the X-ray findings of Béclére. Shows increased depth of frontal sinuses, irregular thickening of the cranial bones, abnormal projection of postlambdoidal eminence, and enlargement of sella turcica.

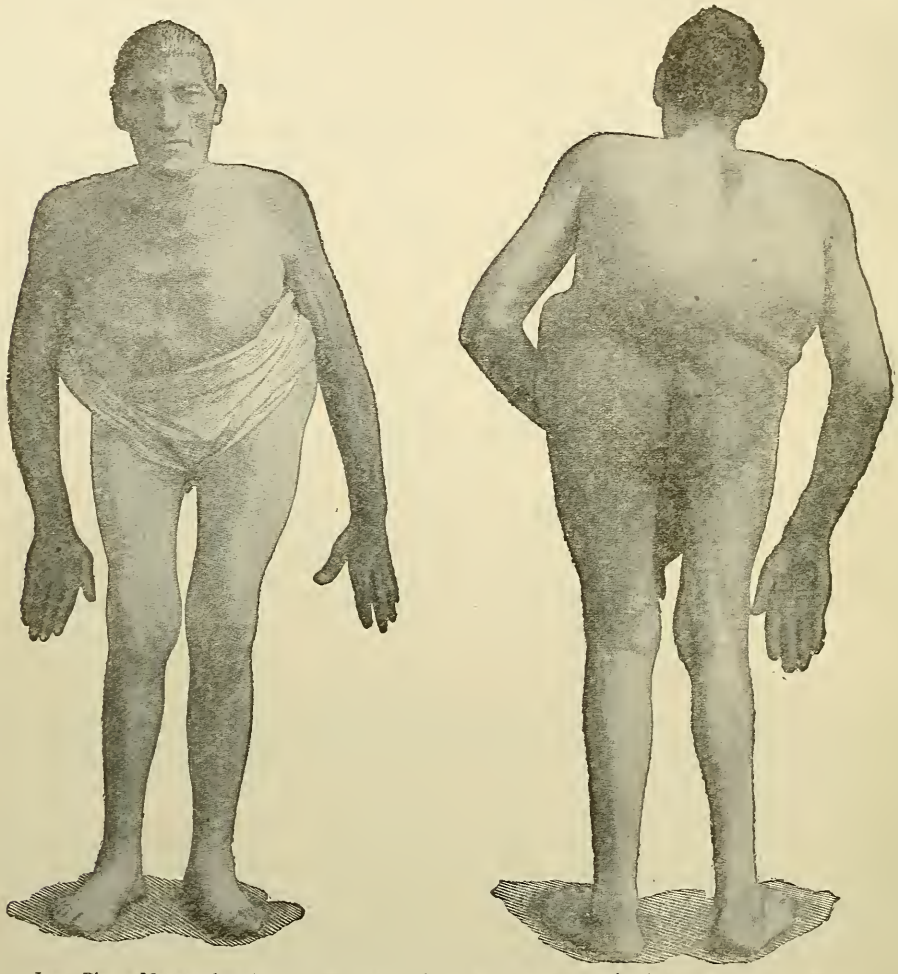
By combining the above data we were enabled to construct a diagram of the acromegalic skull, as shown in the annexed illustration.

By taking X-ray pictures from the facial aspect one can likewise learn of the changes occurring in the mandible and the degree of prognathism they may engender.

German investigators have sought to attain further precision in their radiographic studies. According to von Rutkeroski, each time the hypophysis increases in volume the sella turcica very rapidly enlarges in all dimensions; the distinctions. According to this author, if the tumor remains limited to the sella turcica, the latter enlarges, but its aperture above does not widen. If there is a tumor of the infundibulum, the upper aperture may enlarge, but the bony fossa is little altered. Lastly, if the tumor rises above the sella turcica and bulges out over it, the fossa flares out above, presenting a broad superior opening. We may agree with Furnrohr ("Die Röntgenstrahlen im Dienste der Neurologie," Berlin, 1906) and Sternberg, that these are altogether too fine distinctions. All those who have had oc-

casion to study radiographic prints will readily understand that it is practically impossible to appreciate the trifling differences of shading upon which such distinctions must depend.

interior of the cranium, and that the borders of the sella turcica are clearly apparent. Normally a little cup-like cavity, it becomes so large, when a tumor of the hypophysis is present, that



Jean-Pierre Mazas, the giant of Montastruc (front and back views). (*Brissaud and H. Meige.*)

It is, nevertheless, a fact that the diagnosis of tumor of the hypophysis cannot today be made without the assistance of the X-rays. If, taking advantage of the improved methods introduced by Béclère, we place in the stereoscopic apparatus a reduced image on glass, we find that the body of the sphenoid is brought out in relief in the the tips of two, three, or even more fingers can be accommodated in it.

Relationship Existing Between Acromegaly and Gigantism.—The problem concerning the relationship which gigantism bears to acromegaly is one of great interest. Our data are now sufficiently accurate to allow of its solution.

In his original description, Pierre Marie had clearly separated the two dystrophies. Numerous facts, however, were soon garnered which tended to overthrow this *dualistic view*.

[As early as 1889 Virchow had found reason to state that acromegaly was a secondary condition of degeneration succeeding upon the excessive growth. Langer (Denkschriften der Kaiserl. Acad. der Wissensch. in Wien, xxxi, 1872), Fritsche and Klebs ("Ein Beitrag zur Pathologie des Riesenwuchses," Leipzig, 1884), Cunningham (Trans. of the Royal Irish Academy, xxix, p. 553, 1891), Taruffi (Annali universali di medicini, p. 247, 1879), and Tamburini ("Beiträge zur Symptomatologie und Diagnostik der Hirngeschwülste," Berlin, 1881), in examining the skeletons of giants preserved in the various museums, found the characteristic deformities of Marie's disease, and Massalongo ("Sull'acromegalia," Riforma medica, p. 157, 1892) felt himself justified in concluding, without, however, adducing evidence of his own, that acromegaly was nothing but a delayed, abnormal form of gigantism.

Reports of autopsies, including those of the Peruvian giant, recorded by Dana (Jour. of Nervous and Mental Diseases, Nos. 1 and 2, p. 139, 1893), and of Lady Aama, recorded by Woods Hutchinson, as well as those performed by Buday and Janeso ("Ein Fall von pathologischen Riesenwuchs," Deutsch. Archiv f. klin. Med., p. 385, 1898), and by Caselli, soon afforded a striking demonstration of the intimate relationship existing between the two dystrophies. LAUNOIS AND CESBRON.]

The question was in reality brought to a focus by Brissaud and Henri Meige (Jour. de mèd. et de chir. pratiques, Jan. 25, 1895; Nouv. Iconog. de la Salpêtrière, 1897. Meige, Congrès de Neurol. de Grenoble, 1902, and Archives gén. de Méd., Oct., 1902, p. 410. Brissaud, Bull. de la Soc. Méd. des Hôp. de Paris, May 15, 1896) when they wrote: "The combination of acromegaly with gigantism is far from being a mere coincidence, a casual meeting between two distinct pathological states: Gigantism and acromegaly are one and the same disease. What has not been given sufficient consideration in their reciprocal

Jean-Pierre Mazas, the giant of Montastruc (profile view). (*Brissaud and H. Meige.*)

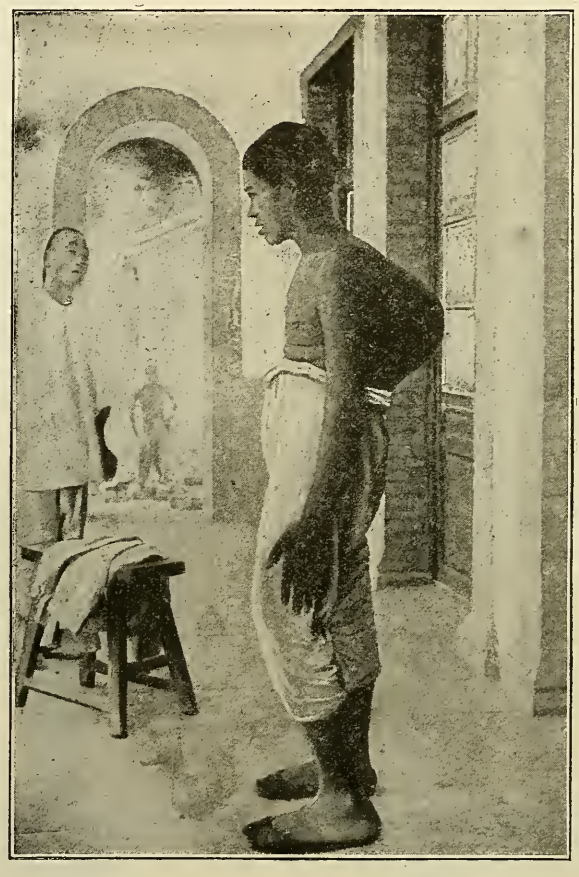
relations, however, is the age at which the disease makes its first appearance. If the stage in which the bony overgrowth occurs belongs to adolescence and youth, the result is gigantism and not acromegaly. If, later on, after having belonged to youth, in which the stature is continually increasing, it en-

croaches upon the period of completed development, *i.e.,* upon that phase of life in which no further osteogenetic growth takes place, the result is a combination of acromegaly with gigantism.

"Gigantism is the acromegaly of the growing period; acromegaly is the gigantism of the period of completed development; acromegalogigantism is the result of a process common to gigantism and to acromegaly, overlapping from the period of adolescence into that of maturity."

These constitute three fundamental propositions, which soon received confirmation from the labors of Woods Hutchinson and of one of us, published in conjunction with Pierre Roy.

As viewed by the adherents of the *unicist theory,* acromegalic gigantism is that form of gigantism in which the characteristic loss of harmony between structure and function finds its expression, to a greater or less extent, in the usual symptoms and deformations of acromegaly, after union of the epiphyses to the diaphyses has taken place, whether this union has been prompt or delayed.



Acromegalogigantism in a Chinaman. (*Matignon.*)

In the majority of giants almost all the stigmata of acromegaly may be recognized. Sometimes but slightly

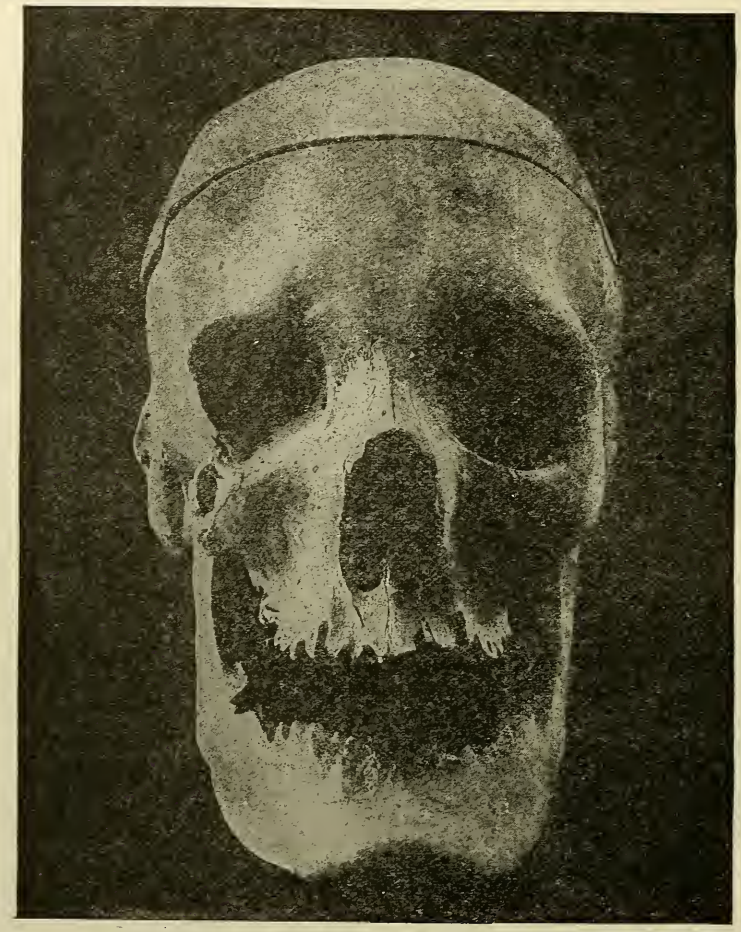
marked, the significant changes can be detected only upon careful inspection; at other times very pronounced, they attract immediate attention and are equally as striking as the stature of the individual afflicted with them. The disproportionate size of the hands and feet; the homely, sometimes even repulsive facial aspect; the evident sagging of the body, which is often marked, make of the subject's gigantic stature a distinction little to be envied, even in the eyes of the layman who cannot recognize the presence of acromegaly in the person before him.

Skull of the giant Constantin (profile view). (*Dufrane and P. E. Launois.*)

[In the cases reported by Brissaud and Meige, Dana, Woods Hutchinson, Byrom Bramwell (Edin. Med. Jour., Jan., 1894, and Brit. Med. Jour., Jan. 6, 1894), Cunningham, Peter Bassoe, Matignon, Launois, and Roy (only the principal ones being here mentioned), the dystrophy had developed to a marked degree. Jean-Pierre Mazas, the giant of Montastruc, studied by Brissaud and Meige, with his undersized skull, projecting superciliary ridges, and well-marked prognathism, his monstrous and grinning face, his abnormally long upper limbs, his enormous hands and feet, his arched back and broadened thorax, recalled precisely the appearance of an anthropoid ape; the morbid state seemed in his case to have brought about a reversion to the ancestral type. LAUNOIS AND CESBRON.]

In the course of our investigations on gigantism we were led to establish a

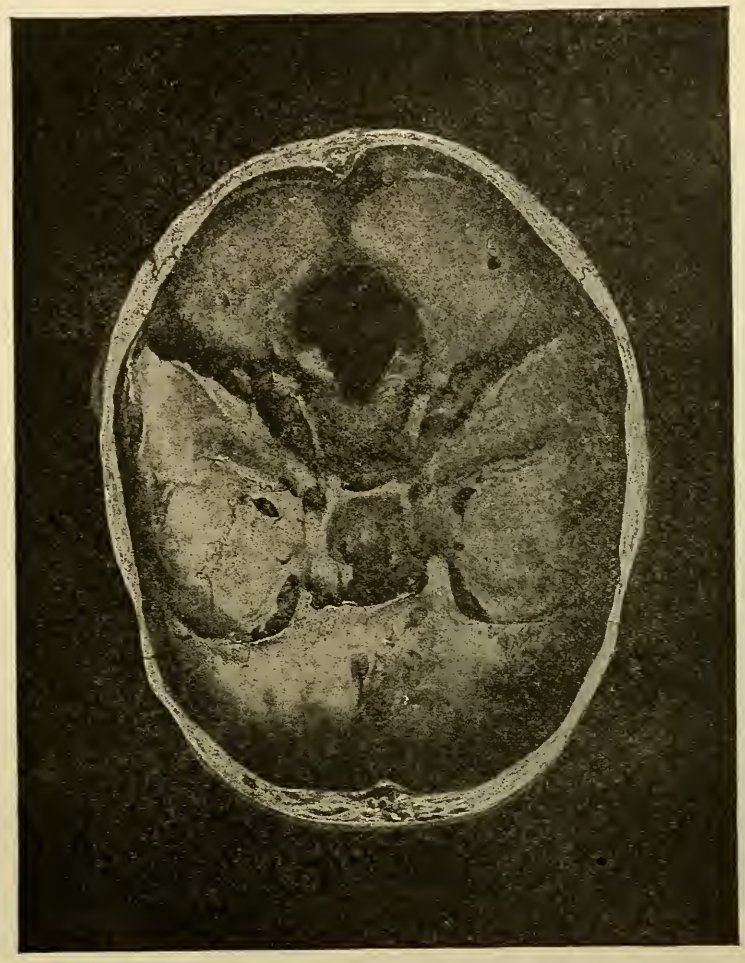
well-defined distinction between two types of giants, viz., the *infantile giant,* in whom the connecting cartilages have not undergone ossification and are still able to proliferate, and the *acromegalic giant,* in whom these cartilages have become ossified and who presents bony thickenings. This distinction, having as its anatomical basis the two separate processes of cartilaginous and periosteal ossification, though a true one morphologically, does not hold good indefinitely in time, *i.e.,* the infantile type, having remained pure during a certain number of years, tends to progress toward the acromegalic type, later merging into it completely. We may state, as a general conclusion, that, while all giants are not acromegalics, at least all those who are not such already are apt to become acromegalics.



Skull of the giant Constantin (anterior view). (*Dufrane and P. E. Launois.*)

[Though able, in the case of the giant Ch——, to follow the fusion of two morphologically distinct types into a single type, we found it impossible to state the exact time at which this fusion took place. Becoming more and more evident as the cartilages bordering on the epiphyses diminish in thickness and become ossified, the fusion reaches completion when the epiphyses have entirely, or almost entirely, united with the diaphyses. In the skull,

face, and extremities the acromegalic deformities then make their appearance and subsequently undergo progressive development. At the autopsy both the stigmata of infantilism and the changes pertaining to acromegaly proper are recognized. In



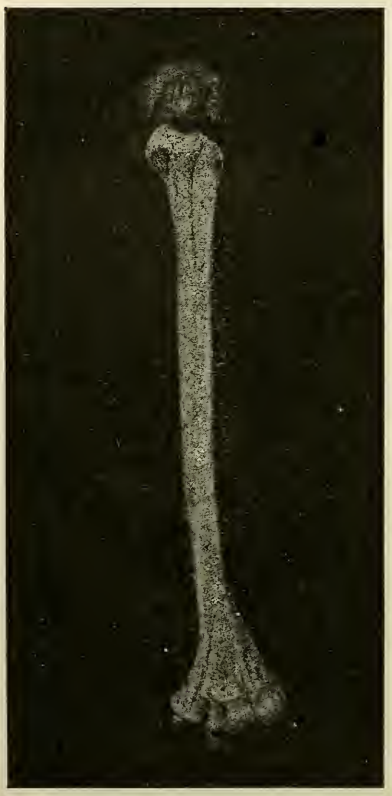
Base of cranium of the giant Constantin, showing marked enlargement of sella turcica. (*Dufrane and P. E. Launois.*)

this connection studies carried out on the body and skeleton of the giant Constantin, preserved by Dufrane in the hospital at Mons, yielded striking results. The illustrations showing his skull and humerus will convey more to the reader than would a lengthy description. LAUNOIS AND CESBRON.]

Whatever be the variety of gigantism encountered, a properly conducted clinical analysis will disclose the morbid manifestations of the hypophyseal syndrome. That this is true is due to the fact that *in all giants,* whether in life by means of the X-rays, or after death on the autopsy table, the existence of a tumor of the hypophysis can be recognized. In 10 cases, taken from among the most recent and the most thoroughly recorded we could find, it was not once lacking. To these direct observations should be added the results obtained from studies of the skeletons of giants. Langer reports having found an in-

crease in the length, breadth, and depth of the sella turcica in every case, and it is well known that in pathological states, as well as normally, the dimensions of this bony fossa in the sphenoid are those best suited for its contents.

The general conclusion warranted by



Humerus of the giant Constantin. Absence of union of upper epiphysis at the age of 29 years. (*Dufrane and P. E. Launois.*)

all these mutually confirmatory data is that, *whether associated with infantilism or acromegaly, gigantism always occurs in association with a tumor of the hypophysis.* This assertion cannot, of course, be given as applying to all future observations, but in view of its uniform confirmation by those of the past it is, at least, very impressive.

COURSE AND DURATION.— Established acromegaly is generally observed in adults, male or female. The initial dystrophic phenomena appear at the age of 18 to 25 years, *i.e.*, at the period in which, under normal conditions, growth is continued and completed. Sometimes it is headache which leads the subject to consult a physician. Other victims, frightened at seeing their hands and feet grow larger, come to find out the reason for these changes. In women the outset of the disease may be traced with some degree of probability to a period at which menstruation became irregular or ceased. We must recognize that such indications are rather vague, as is also the information obtained from the past morbid history. Sometimes infectious diseases are found to have existed, and under these conditions the question arises in our minds whether they could not have created a disturbance in the hypophysis, as well as in the other ductless glands.

The dystrophy seems to occur with greater frequency in women than in men. Taking the combined statistics of Souza-Leite and of Duchesneau, we find 22 men were affected as against 31 women.

While the onset of the disease is sometimes delayed (forty-nine years in a case of Schwartz), it can also be precocious, and the few cases of this kind recorded have made it possible to describe *the acromegaly of children* or *of adolescents.*

[Virchow, in 1889, observed it in a girl 11 years of age; Beaven Rake (British Med. Jour., 1893) reported the case of a young negro; similarly, Valdès-Surmont (Presse médicale, Sept. 22, 1897) saw the first stigmata appear at 14 years. Moncorvo recently reported the case of a girl 14 months old he had observed. This au-

thor does not, however, believe that the disease was congenital, and merely states that everything points to its having become established very soon after birth. LAUNOIS AND CESBRON.]

Race is without influence in the etiology. Acromegaly has been met with in all countries and among all races. Direct hereditary transmission has been observed.

[The observers referred to are Bonardi, Cyon, Schwoner, and Fränkel. E. Schaffer (Neurol. Centralbl., April 1, 1893) recently reported a case of transmission from mother to daughter. Friedreich claims to have observed the stigmata of acromegaly in two brothers. LAUNOIS AND CESBRON.]

The dystrophy follows a progressive, but extremely slow course, which can be divided into several stages. The first (stage of onset), in which the deformities begin to develop, is followed by a second (sthenic stage), in which they attain their maximum. In this stage the acromegalic woman presents a most striking appearance. The increased size of her body, accentuated by hypertrophy of the extremities; her peculiar countenance, with the lips, chin, and cheeks frequently covered with long, curly hair, and her low-pitched voice, all combine to impart a masculine appearance, which is sometimes very pronounced. In a third stage the hypophyseal syndrome asserts itself until its manifestations are more or less completely present.

The *duration* of the disease varies within wide limits (twenty to thirty years). In this connection Sternberg recognizes three forms of the affection: an ordinary form, running its course in eight to thirty years, and two rare forms, the one benign, which may last fifty years, the other malignant, destroying life in three to four years. This last form, seen only 6 times out of 210 cases, is always associated, according to Gabler, with an epithelial tumor of the hypophysis.

PROGNOSIS.—As for the termination, it is fatal. The patient at last invariably succumbs, either to the effects of a slowly developing cachexia, to intercurrent disease, or suddenly succeeding an attack of syncope or some cerebral accident.

If acromegaly be associated with infantile gigantism, the data at hand are somewhat more precise, and the onset of the disease can readily be referred to the growing period proper.

DIAGNOSIS.—The external appearances of acromegalics are so characteristic that the diagnosis is at once manifest, even from a distance. There are a few disorders, however, with which acromegaly might be confounded, and which it is necessary to differentiate.

In *myxedema,* the trunk and extremities show enlargement, which consists, however, merely of an edematous infiltration of the soft tissues. The thickened skin is bound down to the subjacent layers and merges into them. The round, puffy face of myxedema differs radically from the ovaloid face of the acromegalic patient, in whom, besides, prognathism and kyphosis are characteristic features.

In *Paget's disease* of the bones (*osteitis deformans*) there is increased thickness of the cranial bones and more or less marked bowing of the bones of the extremities. The thickened femora and tibia are strongly curved inward and forward, the legs are widely separated, and the trunk and neck are fixed in a position of pronounced flexion. In this affection the bones of the cranium are those involved, whereas in acromegaly the facial bones are rather affected. In the limbs the changes are limited to the

diaphyses of the long bones, whereas acromegaly shows a marked predilection for the bones of the extremities and the extremities of these bones. Paget's disease, moreover, seldom appears before the age of 40, and, differently from acromegaly, attacks the various bones without order or symmetry.

Under the name of *leontiasis ossea* Virchow described a condition associated with hyperostosis of the facial and cranial bones. The lumpy appearance of the exostoses and the normal proportions of the hands and feet are sufficient to preclude all doubt as to the nature of the affection.

In *erythromelalgia* the face remains unchanged. The hypertrophic process involves only the soft tissues of the feet and hands, and is associated with an altogether peculiar cyanotic hue of the integument.

Certain cases presenting a combination of the *stigmata of rickets and of the lymphatic diathesis* might be taken for acromegalics. They exhibit clumsy hands and large feet, the lower lip is thickened and everted, and the face is somewhat puffy. But the extremities show nodal deformities of a special type, while prognathism, as well as macroglossia, are completely absent.

It is in *hypertrophic pulmonary osteoarthropathy,* the dystrophic affection seen among inveterate coughers, that confusion with acromegaly most readily arises.

Pierre Marie, who was the first to recognize and describe this form of systematized osteopathy, showed clearly, in a striking comparison he made of the two conditions, that the features wherein they differ are more numerous than their points of similarity. In both affections there is symmetrical hypertrophy of the upper and lower extremities, together with spinal curvature. But in pulmonary osteopathy, the hypertrophy, which is not uniformly distributed, is associated with distinct deformity of the parts affected. The spinal curve is altogether different from that of acromegaly, and prognathism is absent. The changes are strictly confined to the bony tissues. In the hands, the distal phalanges are clubbed, resembling drumsticks; the nails are lengthened, broadened, curved like a parrot's beak, and show cracks and longitudinal striations.

The carpal and metacarpal regions are practically normal. The wrist, however, is thickened and greatly deformed. In the feet, the distal phalanges are clubbed, the tarsus and metatarsus relatively normal, and the malleoli hypertrophied in all dimensions to such an extent that the lower part of the leg is thicker than the middle. In addition, all the long bones of the limbs are thickened, though more markedly in the leg and forearm than in the thigh and arm. The joints are involved in these changes; their enlargement interferes with ease of motion, both active and passive. Furthermore, kyphosis is not constantly present, and when it is present is confined to the lower dorsal or lumbar regions. In the face, the superior maxillary bone is alone thickened, the mandible remaining normal.

Pulmonary osteoarthropathy may give rise to some little difficulty in diagnosis, principally owing to its rarity. It is most likely to be confounded with acromegaly, but in the latter disease there is no alteration of the nails, nor are the finger-ends nor the carpus and metacarpus much thickened. The chief characteristics of the disease are great enlargement of the hands, wrists, feet, and ankles, associated with, and secondary to, some chronic pulmonary affection, such as phthisis, chronic bronchitis,

and empyema. In the joints the changes are effusion with enlargements and ulceration of the cartilages and articular ends of the bones. Marie is of the opinion that these changes are due to toxic poisoning, but Thorburn looks on them as tuberculous. The evidence either way is slight and indefinite. G. A. Bannatyne (Lancet, Feb. 23, 1901).

In *syringomyelia of the pseudoacromegalic type,* the hypertrophic process is confined to the upper limbs and sometimes to a single extremity. It does not involve equally all the fingers of a hand. The parts involved are deformed and exhibit more or less marked trophic changes. The symptoms resulting from the spinal cord lesion are easily recognized.

As for certain *localized hypertrophic manifestations* (macrodactylia, macropodia, hypertrophy of a limb, or of one side of the body), described by Virchow under the name of partial acromegaly, they are congenital in most instances and bear no relationship to true acromegaly.

PATHOLOGY.—The dystrophic process in acromegaly shows a special predilection for the supporting tissues derived from the mesoderm (connective tissue, cartilage, and bone), to whatever degree of differentiation they may have attained.

The thickening of the integument is due to marked proliferation of its connective-tissue elements; the proliferation takes place in each of its various layers. Hyperplasia in the superficial stratum brings about hypertrophy of the papillæ, causing them to appear as pronounced ridges. Similar connective-tissue proliferation takes place in the walls of the sebaceous and sweat glands, in the sheaths of the hair-follicles, in the adventitia of the superficial blood-vessels, and in the nerve-sheaths. These vascular and nervous changes are not without influence on the trophic state and functions of the skin. They likewise interfere with the nutrition of the cutaneous appendages. The epidermis develops many new layers, especially in the zone of the stratum corneum; the several varieties of hair become thickened and kinked, and the nails develop longitudinal striations. Hypertrophy of the teeth has occasionally been noticed (Henrot).

The connective-tissue cells of the subcutaneous panniculus adiposus in some cases become overloaded with fatty material. To this superficial adipose deposit is added, in the syndrome identified by Fröhlich, a deep-seated adipose accumulation, especially marked in the neighborhood of the peritoneal reflections.

Macroglossia is due not only to thickening of the mucous covering layer of the tongue, but also to abnormal growth of the interstitial connective tissue. The nasal, pharyngeal, laryngeal, and tracheal mucous membranes are likewise the seat of marked proliferation of the connective-tissue elements.

The alterations occurring in the fleshy portions of the muscles must also be attributed to changes of this kind. Thickening of their sheaths and of the septa dividing them into bundles brings about a marked increase in their size. Microscopically, proliferation of the nuclei and atrophy of the contractile substance are observed. The hypertrophic process extends to the tendons, of which the inserting surfaces become broader, and to the aponeurotic expansions.

Among all the changes which the supporting tissues undergo, the most characteristic, as well as the most marked, are those involving the skeleton; they

are the result of a disturbance in the process of periosteal bone formation.

They are met with in the bones having marrow cavities, and are confined to those of the extremities and those of cancellous structure. They are also found in those membranous bones (cranial bones, inferior maxillary bone) which develop directly from the connective tissues, without being preceded by cartilage.

Whereas in adult life the periosteum ordinarily ceases to be productive except under certain experimental or traumatic conditions, of which a detailed analysis was made by Ollier, in acromegaly it is seen to proliferate and produce increased thickness of the bones by laying down new osseous layers. Pierre Marie and Marinesco (Archives de Méd. Exper. et d'Anat., p. 539, 1891), Renaut and Duchesneau, have made studies of the histological changes occurring in this abnormal type of osteogenesis. The process is described as "a slow growth of certain bones, taking place at the expense of the periosteal bone, which is reduced to thin layers, while the bony tissue of medullary origin gains in prominence, continues to develop with, so to speak, mathematical regularity, and comes to occupy a predominant position in the structure of the bone. On transverse section the entire area is occupied by red bone-marrow, containing more or less numerous fat-cells. The vessel supplying each medullary space is located exactly in its center and appears in cross-section. . . . At the periphery of the bone-marrow, in the neighborhood of the open areas corresponding to the giant Haversian spaces of cancellous bone-tissue, the rows of osteoblasts and multinuclear cells which are seen in rachitic bones are here conspicuously absent."

Summarizing the above, we may state that, whereas new layers are being added at the periphery of the bone, the central portion is undergoing actual resorption by the osteoclasts, the marrow proliferating to take its place. Recently Presbéanu (Thèse de Paris, 1909) had the opportunity, in a case of acromegaly that died as the result of a fall causing multiple fractures, to note the existence of marked demineralization of the bones; the proportion of ash, which normally ranges between 50 and 80 per cent., had been reduced to 36 per cent. These chemical changes may well account for the weakened condition of the skeleton in this disease.

In infantile giants undergoing transition into acromegaly, the changes in the bones coexist with an altogether abnormal persistence of the cartilages uniting the epiphyses of long bones to their diaphyses. In these cases the bones, while growing in thickness, also increase in length, at least for a certain period.

The articulating surfaces of the bones become broader, and the cartilaginous tissues covering them spread out without losing in depth. They may undergo some slight alterations in structure, recalling those seen in the early stages of certain arthropathies.

As for the changes occurring in the cardiovascular system, though less plainly evident than those already discussed, they are, nevertheless, well marked. The thickening of the vessel walls and cardiac hypertrophy are due to hyperplasia of the connective-tissue elements they contain. The cardiac muscular fibers may be more or less altered.

> Enlargement of the heart, either simple or associated with a myocarditis, is the condition usually found in acromegaly. Sclerosis of the arteries and degenerative lesions affect-

Molds of the Upper Extremities of a Case of Acromegaly. (*P. E. Launois.*)

ing the walls of the veins, with dilatation and subsequent obliteration of their lumen, are constantly present. These changes in the heart and vessels should be considered as much a part of the clinical picture as the changes in the bones, and they are probably due to the prolonged hypertension of the vessels, the result of hypersecretion of the pituitary body. Phillips (Med. Rec., Feb. 20, 1909).

The spleen and lymph-nodes sometimes appear sclerosed, so greatly has their connective-tissue network become thickened.

In a few cases a more or less generalized condition of splanchnomegaly has been reported, constituting a genuine gigantism of the viscera.

[In this connection the observations of Linsmayer, of Bourneville and Regnault (Bull. de la Soc. Anat. de Paris, July 31, 1896), and of Chauffard and Ravaut (Bull. de la Soc. Méd. des Hôp. de Paris, Mar. 23, 1900) have yielded valuable information. LAUNOIS AND CESBRON.]

The kidneys, spleen, and pancreas had, in a few of these cases, doubled or even tripled in size.

Atrophy of certain viscera, *e.g.*, of the kidney, has been recorded in a few cases; the appearance of the renal cortex recalled that commonly found in interstitial nephritis.

In the nervous system the connective-tissue proliferation already manifested in the finer peripheral divisions then extends to the deeper branches of the nerves, which present the appearance of thick cords. The sympathetic nerve branches, and more especially the inferior cervical ganglion, have been found enlarged and sclerosed.

In a case studied by Duchesneau, the peripheral nerves showed changes due to pressure exerted on the spinal roots at the intervertebral foramina. In that of Sainton and Staté there was bony infiltration of the dura, with the formation of calcareous deposits on its inner surface, transforming it, in the dorsal and lumbar regions, into a veritable tube of lime.

The spinal cord has occasionally been found the seat of connective-tissue proliferation and localized or more or less widespread sclerosis.

In the brain, the neuroglia, which is also one of the group of supporting tissues, may proliferate more or less actively.

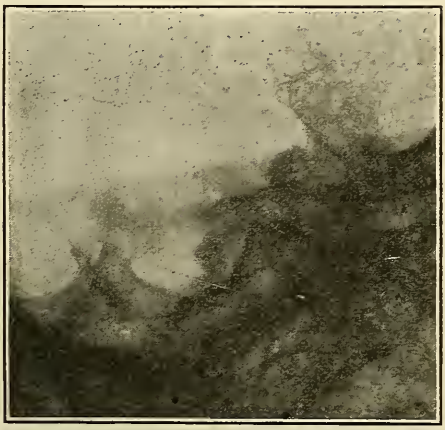
The Hypophysis.—Among the changes taking place in the intracranial structures, the most interesting, as well as the most important, are those involving the hypophysis.

Connected by a partially hollow stalk with the base of the brain, molded into the sella turcica, which it almost completely fills, held in position by a diaphragm of dura mater centrally perforated, and weighing on the average 0.5 gram [7½ grains] in adults, the hypophysis has long been considered an ancestral remnant, a rudimentary organ of no importance.

[Modern histological researches, in particular those of Comte (Thèse de Lausanne, 1898), of Caselli, of Benda (Berliner klin. Wochenschr., No. 52, 1900; Neurol. Centralbl., p. 140, 1901, and p. 223, 1902; Archiv f. Psych., xxxv, p. 272, 1901), of Launois (Thèse de la Faculté des Sciences de Paris, 1904), of Thaon (Thèse de Paris, 1908), of Gentès (Bull. de la Station biologique d'Arcachon, 1907), of Joris ("Contribution à l'étude de l'hypophyse," Mémoire couronné publié par l'Académie royale de Bruxelles, xix), etc., have furnished an insight into the structure of its two constituent parts—the epithelial lobe and the neural lobe. LAUNOIS AND CESBRON.]

According to one of us, the anterior or epithelial lobe of the hypophysis is a gland of branched tubular type. The epithelial tubes or cords of which it is

composed undergo anastomosis. In the spaces between them run very broad capillary blood-vessels, with very thin endothelial walls, which must be considered as the excretory ducts. The glandular cords are made up of epithelial cells loaded with granulations. In view of the different staining affinities shown by the latter, the cellular elements containing them may be divided into three classes: 1, acidophile cells, which may be eosinophiles, fuchsinophiles, or aurantiophiles; 2, basophile cells, sometimes called cyanophiles; 3, chromophobe cells. The protoplasm of these cells is always acidophile. It contains, except in the case of the young acidophilic forms and the chromophobes, zymogenic granulations, which infiltrate the epithelial elements of the glands. In addition to their acidophilic property, the intracellular granulations possess in common the property known as siderophilia.



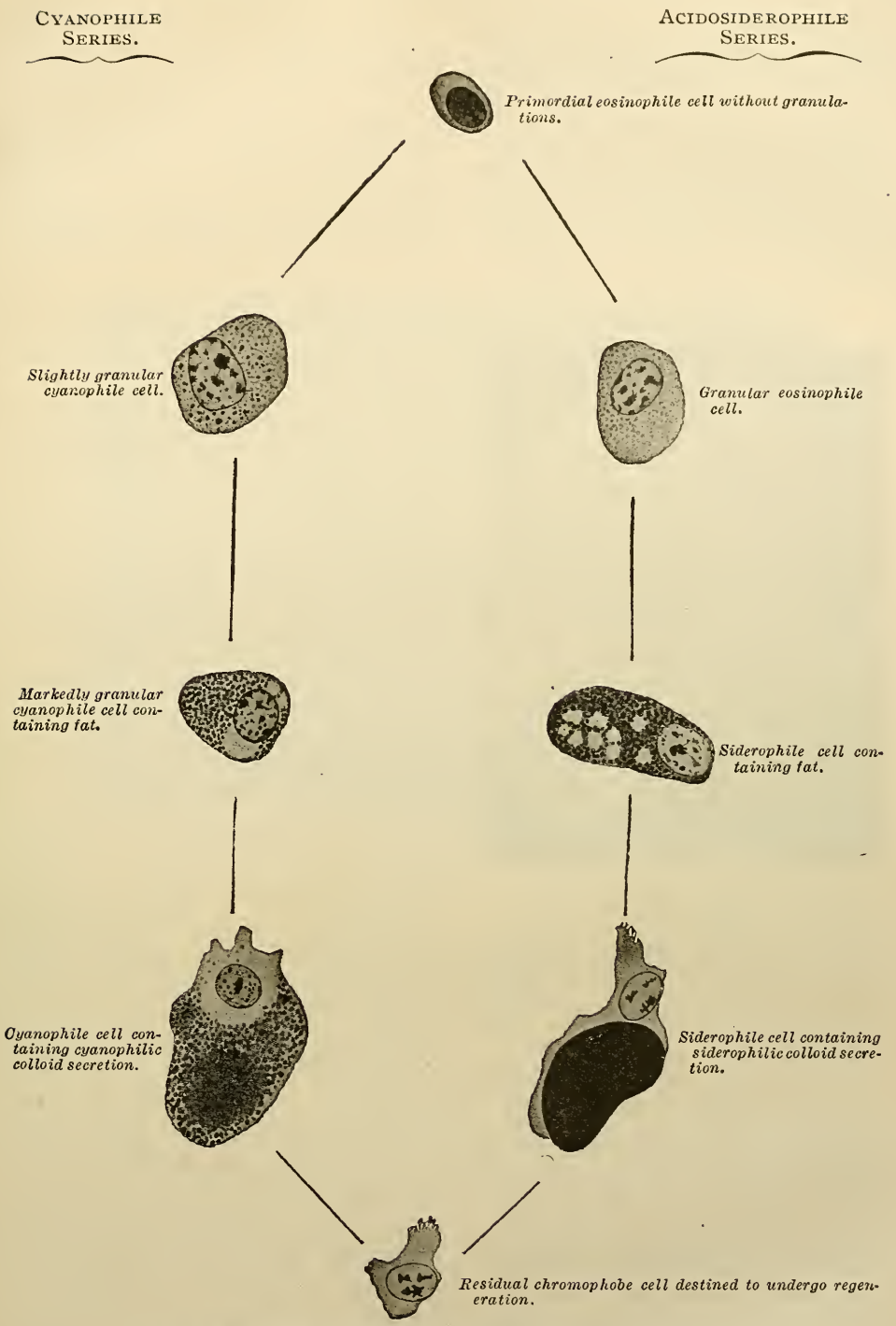
X-ray of base of an acromegalic cranium, showing enlargement of sella turcica. (*Ch. Infroit.*)

The primordial cell of the pituitary gland, from the morphological as well as the embryological standpoint, is a small eosinophilic cell with compact nucleus and small protoplasmic body, devoid of granulations. This cell develops along two different lines and produces either an acidophilic and siderophilic secretion or a basophilic secretion. Two distinct series of cells, therefore, exist in the hypophysis: an eosinophilic series, which becomes siderophilic, and an eosinophilic series, which becomes basophilic. The products elaborated by them having been eliminated by a semiholocrine process, the cells of both series become chromophobic cells, which are capable of undergoing regeneration and of renewing their functional activity. The secretory product of the hypophysis is a colloid substance, giving reactions sometimes acidophilic, at other times basophilic, and which presents analogous features with the material contained in the alveoli of the thyroid gland. We have thought it proper to introduce a summary of this cytologic study, based on our own researches, believing that it may serve as a basis for pathological studies, the results of which thus far have been indefinite and inconstant.

On the basis of facts discovered on the autopsy table, which today usually receive confirmation from radiographic studies of the skull during life, we are able to assert, as we have already shown, that hypertrophy of the hypophysis is the rule in acromegaly.

[We need but call to mind the statistics of Woods Hutchinson, based on a series of 48 cases. In 44 of these the autopsy revealed a more or less marked enlargement of the gland and a corresponding increase in the size of the sella turcica. Of the 4 cases in which no enlargement was found, 3 could hardly be considered as cases of true acromegaly (those of Scarbo, of Friedreich, and of Arnold). In the fourth, that recorded by Bonardi, the gland seemed morphologically normal.

Similarly, Modena, out of 70 cases with autopsies recorded, found hypertrophy of the hypophysis in 65. In but 5 cases did



The two series of secreting cells found in the hypophysis, according to the researches of P. E. Launois.

the organ appear to be of normal size, and in only 1 [Labadie-Lagrave and Deguy (Archives gén. de Méd., Feb., 1896)] did it seem likewise normal in histological structure.

Caussade and Laubry (Archives de Méd. expér. et d'Anat. pathol., p. 172, Mar., 1909) have more recently collected the information scattered in literature concerning cases in which a tumor of the hypophysis was not accompanied by acromegaly or osseous hypertrophy. Schüster, in 62 cases

Tumor of the pituitary from the giant Santos. (*Dana.*)

of tumor of the hypophysis accompanied by mental disturbances, reports having found acromegaly but 12 times. LAUNOIS AND CESBRON.]

We desire to call attention to the fact that in a number of these negative cases the tumor did not originate in the hypophysis itself; that this gland was simply compressed or destroyed, and that in a few cases the histological descriptions were decidedly lacking in completeness. We must admit, nevertheless, that certain of the facts at hand leave room for doubt, which will have to be dispelled by future observations.

The gross features of tumors of the hypophysis vary. The size ranges from that of a cherry up to a hen's egg or mandarin. The sella turcica varies similarly in its dimensions; its clinoid processes recede from one another, become blunted, and, where an infiltrating neoplasm is present, sometimes disappear entirely, together with the bony partitions they surmount.

The tumor not infrequently projects beyond the limits of the bony fossa, notwithstanding the increased size of the latter; it bulges toward and indents the lower surface of the cerebrum, and may even infiltrate it to a considerable depth.

In color the growth is usually grayish, sometimes yellowish; its external surface, often granular in appearance, may be dotted with small, reddish areas, representing dilated vessels or even true hemorrhagic foci. In consistency it is soft and more or less friable. On complete transverse section more or less extensive pockets of colloid material having a gelatinous appearance may be revealed.

These general features, which belong more particularly to tumors of epithelial origin, may be variously modified according to the type of neoplasm present, which may be sarcomatous, angiomatous, etc.

The minute structure of tumors of the hypophysis has been variously interpreted. The diversity of the descriptions given of it results chiefly, if not entirely, from the uncertainty which prevailed until within the last few years as to the normal structure of the gland.

It seems to have been shown, however, that, in a number of the cases reported, the tumor was epithelial in origin. From the 57 cases collected by him, Parona has obtained the following percentages:—

Adenosarcoma	45	per cent.
Adenoma	26	" "
Sarcoma	19.4	" "
Angioma	3.4	" "

These figures, together with similar statistics already published, should be taken with some reserve, and we must recognize, with Hanau, that the condition of diffuse hypertrophy of the pituitary which, while normal in macroscopic appearance, contained numerous large chromophilic cells.

[Similarly, Gilbert Ballet and Laignel-Lavastine (Nouv. Iconogr. de la Salpêtrière, p. 176, 1905) have noted in acromegalics at the outset a glandular hyperplasia in course of development. LAUNOIS AND CESBRON.]

Tumor of the pituitary body extending into the right lateral ventricle. (*P. E. Launois.*)

tary bears a marked resemblance to sarcoma.

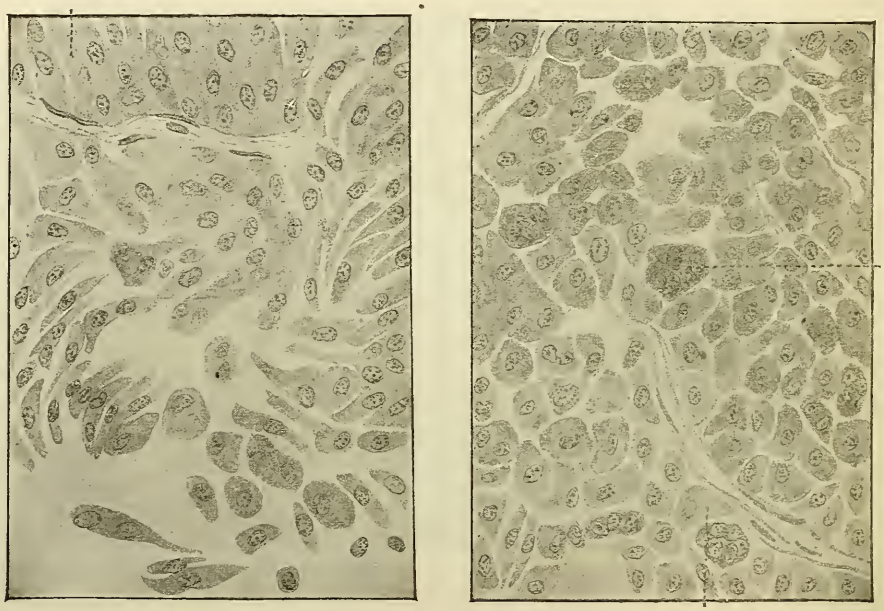
A few of the descriptions, however, embody cytological details sufficiently definite to be of value. Among them may be mentioned the observations of Benda, who found, in three instances, that the hypertrophy was due to proliferation of the chromophile cells, *i.e.*, the functionally active elements of the gland. In a fourth case, the neoplasm was undergoing regression. Hyperplasia of the same cells has likewise been observed three times by Vassale. Lewis, in an acromegalic case which succumbed to cerebral hemorrhage soon after the onset of the dystrophy, found a pituitary

Case of acromegaly of ten years' duration. No enlargement of the hypophysis was found at autopsy, but, instead, a tumor composed of tissue identical with the chromophile cells of the anterior lobe of the hypophysis, and occupying the body of the sphenoid bone, immediately beneath the sella turcica. Supports theory of Tamburini and Benda that acromegaly is caused by a hypersecretion of the hypophysis. Erdheim (Ziegler's Beiträge, Bd. lxiv, S. 233, 1909).

Enlargement of the hypophysis may also result from exaggerated growth of its connective-tissue network. Under such conditions the stage of hyperplasia of the organ, associated with expansion of the sella turcica, may be followed by

a stage of sclerotic atrophy. The enlarged bony cavity does not resume its former size and appears too capacious for the gland inclosed in it. This condition was found in a case of Huchard, in which the autopsy was performed by one of us.

Instead of being generalized throughout the glandular parenchyma, the neoplastic process may be localized and appear in the form of more or less voluminous masses (partial adenomas, cysts), reaching a variable size [Widal, Roy, and Froin (Revue de Méd., Apr. 10, 1906)].



Cellular characteristics of a tumor of the pituitary. (*P. E. Launois.*)

From a general review of the facts yielded by recent investigations, the tendency has arisen to accept the conclusion that the hyperplastic condition of the hypophysis observed in acromegaly is dependent upon an increase in the number and size and an exaggerated functional activity of the chromophilic cells. This assertion, however, which to us appears premature, cannot, at present, be unreservedly accepted, for a few cases have been seen in which the hypophyseal lesion was not accompanied by any dystrophic disturbance.

In acromegalic gigantism tumors of the hypophysis are more constantly present than in simple acromegaly. We have already stated, indeed, that in the former condition they have never been found wanting. As for their histological structure, the same uncertainty prevails.

To complete this study, we shall mention the alterations which the other ductless glands may undergo in acromegaly:—

With reference to the thyroid, Hinsdale, in a series of 36 cases collected from the literature, found hypertrophy 13 times, atrophy 11 times, while in 12 cases the gland appeared to be normal.

[According to Furnivall (Pathol. Soc. of London, Nov. 2, 1897), the thyroid seemed

normal in only 5 out of 24 cases of acromegaly. We have ourselves seen the dystrophy coexisting with simple goiter; Lancereaux and Murray (Edin. Med. Jour., 1897), with exophthalmic goiter. LAUNOIS AND CESBRON.]

Klebs, Massalongo, and Mossé have reported hypertrophy or regeneration of the thymus gland. Most observers have failed to inquire into the condition of the adrenals. Their study might prove fruitful, in view of the opinion of Sajous that these organs take an active part in the morbid process.

PATHOGENESIS.—According to Klebs, who had witnessed persistence of the thymus in a case of acromegaly, the affection is due to an unusual state of development of the vascular system, and results from an angiomatous condition of the thymus. According to this view, the thymus produces endothelial elements which, swarming through the vessels, assume the rôle of formative cells in the production of fresh vessels. Thus there would result an increase in the number of vascular channels, and, in consequence, hypernutrition and augmentation in size of the terminal portions of the body, *i.e.*, of those regions of the organism in which the flow of blood slackens its speed. This power to form new vessels, however, which he attributes to the thymus, is as yet lacking in proof.

Massalongo has taken up Klebs's theory and modified it. He believes acromegaly to be due to persistence of the functions of the thymus and the hypophysis—organs which play an important part during fetal life. Normally, these glands undergo retrogression, he states, at the age when growth ceases, *i.e.*, between the 20th and 25th years. If their functions continue after that age has been passed, acromegaly results.

Freund and Verstraeten attribute the dystrophy to a reversal in the normal order of events occurring in sexual development. "In a certain number of individuals," writes Freund, "the ordinary mode of development is disturbed. Either it lags behind the norm, or else it advances beyond the norm, both in time and in space [*i.e.*, morphologically]; the malformations which result go hand-in-hand with the disturbance in the development of puberty, and later, too, of the sexual functions." It is certain that the development of the genital apparatus is not without influence on that of the osseous system, and one of us, in a series of communications, has described the alterations produced in the bones by congenital atrophy of the testicles, of the ovaries, and by castration before puberty. Now, the frequency with which disturbances of the genital functions are associated with acromegaly has long been noticed. But how is the influence they may exert on the growth of the skeleton to be explained? Perhaps by their suppression, diminution, or modification of a secretory product having as its purpose, as suggested by Sajous, to activate the oxidation of phosphorus-containing substances.

[Schiff, Ruttle, and Duchesneau have reported an increased elimination of phosphorus; but Moraczewski (Zeitschr. f. klin. Med., xliii, Nos. 3 and 4, 1901), Tansk and Vas, and Parhon ("Contributiuni la studiul schimburilor nutritive in acromegalie," Bucuresti, 1903; Revista Stüntelor Medicale, No. 2, 1905), on the other hand, have found it to be retained in the organism. LAUNOIS AND CESBRON.]

In short, the development of the genital functions having some influence on that of the skeleton in general, disturbances in these functions may be factors in the production of acromegaly, but

they do not appear to be sufficient to bring on the dystrophy of themselves.

In the opinion of Recklinghausen and Holschewnikow, acromegaly is merely a trophoneurotic affection, dependent upon changes in the central and peripheral nervous system. Disturbances involving the vasomotor nerves would, according to this view, lead to overnutrition and hypertrophy of the extremities. There is nothing to indicate, however, that the nervous changes in this dystrophy are primary. The case on which these two observers based their opinion was one of syringomyelia.

Pierre Marie looks upon acromegaly as "a kind of systematized dystrophy, occupying in the nosological scale a position about corresponding with that of myxedema, and bearing to an organ of trophic function (the hypophysis) as yet unknown relations similar to those which unite myxedema and cachexia strumipriva to certain lesions and removal of the thyroid gland."

As this quotation shows, it was the sponsor of acromegaly himself who was the first to suspect the functional rôle of the hypophysis, "that enigmatic organ," as Van Gehuchten termed it not so many years ago.

In the preceding pages we have sufficiently dwelt upon the frequency, and even constancy, with which hypertrophy of the hypophysis, especially of epithelial origin (adenoma), is present in acromegaly. We pointed out, likewise, a condition which is daily receiving confirmation from X-ray studies, viz.: that, whatever be the mode of progression of the dystrophy, whether it take expression in its sthenic phase as the pure acromegalic type of Pierre Marie, or the lipomatous type of Fröhlich, there is present in most cases enlargement of the sella turcica, which serves to indicate hypertrophy of the pituitary body. In view of these facts, while recognizing to their full value the negative cases so far recorded, we are completely in favor of the hypophyseal theory.

Having reached this conclusion, we still have to solve two other phases of the problem, viz.: to ascertain the nature and mode of action of the disorders affecting the function of the hypophysis, and to find out whether these disorders are sufficient in themselves, or whether it is not necessary to invoke the synergistic functions of the other ductless glands as participating in the disturbance.

The experiments of physiologists, an excellent analysis of which has been given by Paulesco (L'hypophyse du cerveau, Paris, 1908), have yielded, it must be said, no definite results. Practised upon young or old animals, removal of the hypophysis produced no skeletal disorders nor acromegalic manifestations. This dearth of results is not surprising when we consider, on the one hand, the comparatively short period of survival of the experimental animals, and, on the other, the serious traumatism to which they had been subjected in the operations. Of greater weight, as we have already emphasized, are the data afforded by the clinicopathological method. It is on the basis of these data that investigators have sought to ascertain the functions of the hypophysis, and, in particular, its trophic rôle.

Some authors, among them Tansk and Vas, and Parhon, consider acromegaly to be the result of excessive functionation on the part of the pituitary—a genuine *hyperhypophysia*. According to others, the functional rôle of the gland is to destroy substances toxic to the nervous system. The accumulation of these substances, in the presence

of functional disturbance of the hypophysis, would produce, because of special predisposition, a continual state of irritation, resulting in hyperplastic changes in the bony and other supporting tissues, primarily and chiefly noticeable in the extremities. The acromegalic deformities would be an expression of functional insufficiency of the organ, or *hypohypophysia.*

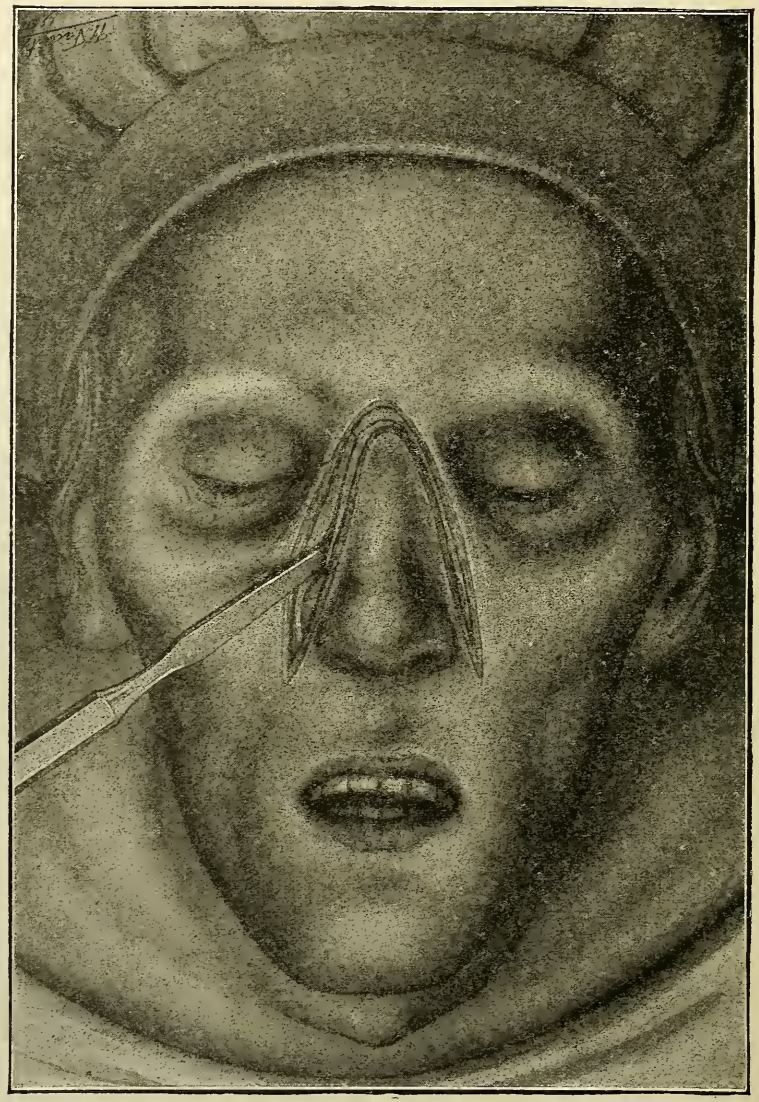
The above hypotheses were those most generally accepted when Hochenegg published the results of his operations of hypophysectomy, which will be described below. The progressive retrogression of the manifestations of acromegaly witnessed after excision of hypophyseal tumors affords an argument of the first importance in favor of the *theory of glandular hypersecretion.* Future observations will soon bring further confirmatory evidence.

The facts recorded by Hochenegg have also lent considerable support to the doctrine of the synergistic functional relationship existing between the ductless glands. In one of his cases, menstruation, which had long since been arrested, returned and was maintained at regular intervals. In 2 cases removal of the hypophysis was followed by hypertrophy of the thyroid. We have already stated that at the autopsy of acromegalics hyperplasia of one or more ductless glands is frequently found. Furthermore, it is well known that the sexual glands exert a distinct influence on the osteogenetic activities of the connecting cartilages, and that thyroid extract is possessed of an analogous action. Caselli has expressed his belief in the identity of the functions of the hypophysis and thyroid, basing his opinion on the experimental observation that removal of the hypophysis acts on tetany parathyreopriva in the same manner as does removal of the thyroid. This functional identity, as Souques ("Acromégalie" in "Traité de Médecine" of Charcot and Bouchard, 2d ed., vol. x, p. 490) terms it, or, better, this functional analogy, would furnish an explanation for the power of mutual substitution of function exhibited by these glands under pathological conditions.

It was through surgery, practised for curative purposes, that the functions of the thyroid were revealed to us; it is through surgery that today the rôle of the hypophysis is being disclosed. It is to surgery, again, that we shall in the future be indebted for the acquisition of positive data which will enable us to solve the absorbing problem concerning the synergistic functional relationship of the ductless glands.

The craniopharyngeal canal, which passes down from the floor of the sella turcica through the basisphenoid into the nasal pharynx, normally becomes obliterated in the fetus at the beginning of the third month. In 4829 skulls it was noted by le Double to be persisting in only 10, about 0.2 per cent. Schlaginhaufen observed it, on the other hand, in 40 per cent. of apes' skulls examined. The interesting fact now comes to light that Dr. Ettore Levi, of Florence, has found it persisting in the skulls of two acromegalics which he has had the opportunity of observing, and he describes the condition in the Revue neurologique for May 15th. In one, situated mesially and at the junction of the anterior and middle third of the floor of the sella turcica, was a round depression 6 mm. in diameter and 6½ mm. deep; at the bottom of this was a small, round opening which communicated by a canal 9 mm. long through the basisphenoid with the nasal pharynx, entering the latter at a point 5 mm. from the posterior margin of the left wing of the vomer, and allowing the passage of a seeker 1 mm. in diameter. In the second case a canal in almost exactly the same

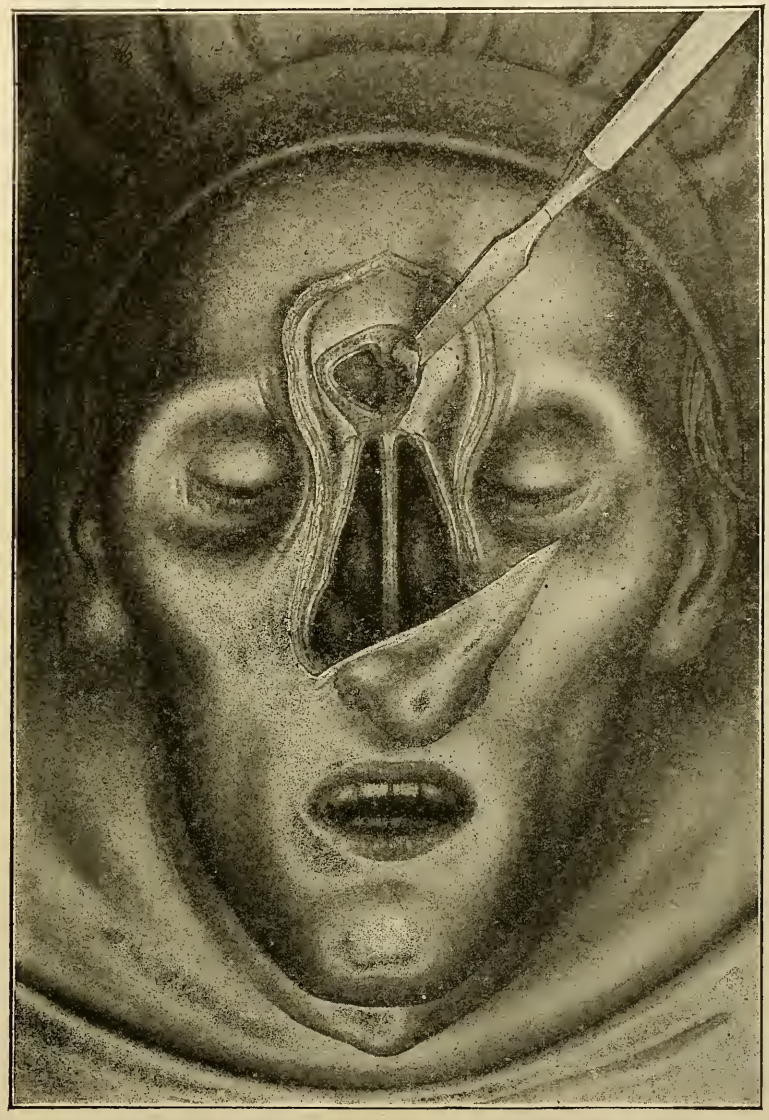
site and with the same course was found. In this connection it is instructive that in the skull of the Irish giant Magrath, described by Professor Cunningham, an elliptical perforation was noted in the floor of the sella turcica communicating directly with the nasal pharynx, the lower end of it being partly covered by the enlarged wing of the vomer. A re-examination of acromegalic crania in view of these facts is called for, as it is quite conceivable that an abnormality of this nature has escaped observation. The light which it may throw on the hypophyseal theory of acromegaly may be considerable. Recent researches have conclusively shown the existence of pituitary tissue in the vault of the nasal pharynx, deep in the soft tissues lining the vault, an accessory pharyngeal hypophysis identical in structure with the glandular part of the



Vertical rhinotomy by means of bilateral osteotomy; Ollier's method. (*R. Proust.*)

cranial hypophysis and of normal and constant occurrence. Its pathology is unknown, and what relation it may bear to those cases of acromegaly without obvious lesions of the pituitary gland, and those other cases of lesion of the pituitary without acromegalic symptoms, is equally unknown. Data such as these suggest an interesting line of research for subsequent investigators. Editorial (Lancet, June 5, 1909).

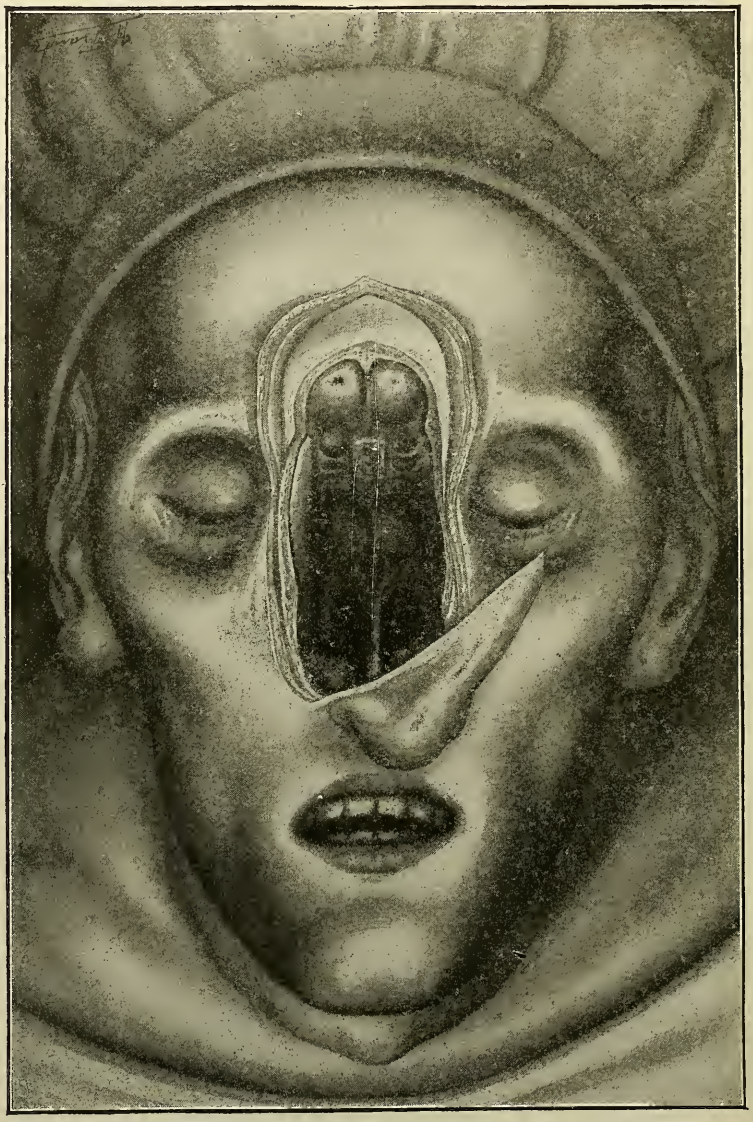
TREATMENT.—The treatment of acromegaly necessarily remained, for a long time, purely symptomatic, and was limited to combating the most distressing manifestations, such as pain and insomnia. Agents modifying general nutrition, such as **iodine** and **arsenic** (Campbell), were then brought into use. **Iron** in large doses and hot baths



Opening of the frontal sinus after deflecting the nose. (*R. Proust.*)

were said to have given distinct relief in a case under the care of Brissaud. Schwartz claimed to have obtained beneficial effects from the use of **ergot.**

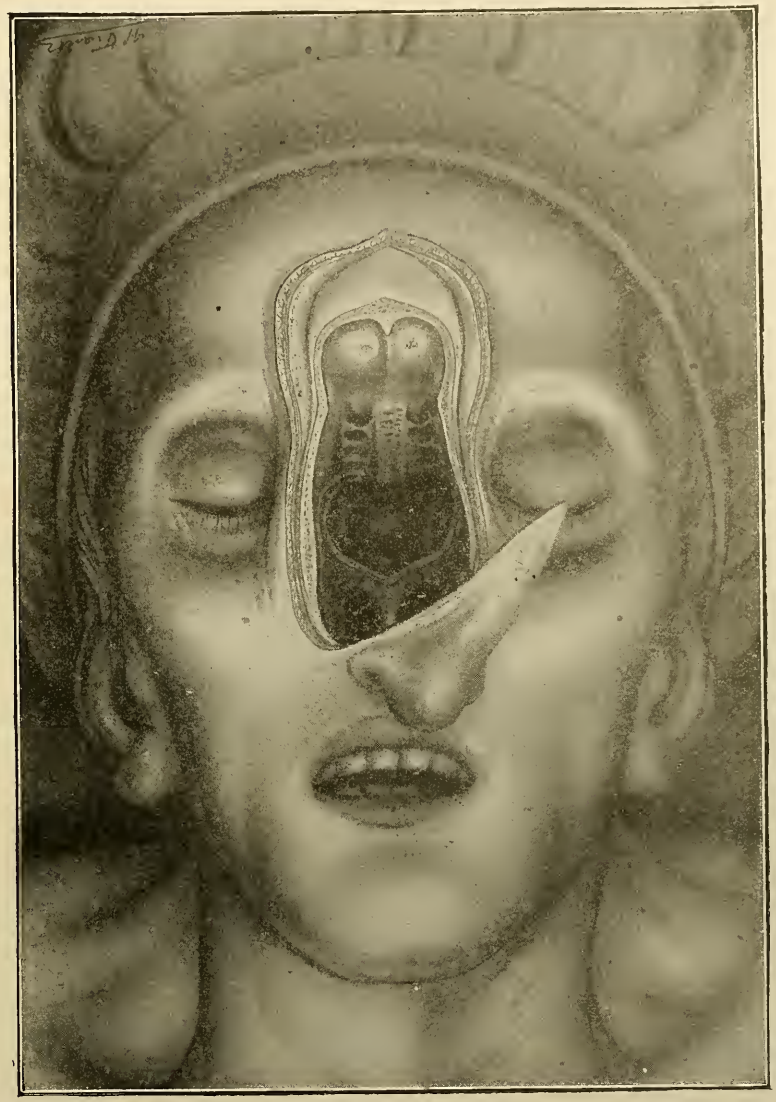
As a corollary to the discoveries of Brown-Séquard, opotherapic medication was resorted to. Warda and Pirie tried **thyroid** treatment without success, though Lyman Greene claimed good results with it. Napier administered powdered **ovary** to an acromegalic woman without benefit. Kuh, using **pituitary** substance, and Favorsky, using Poehl's opohypophysine, noted distinct improvement in the



Approach to the sphenoid after resecting the ethmoid and clearing the nasal passages. (*R. Proust.*)

subjective, and even the objective, symptoms. The latter observer was able to continue the administration of **hypophysine** in daily doses of 0.05 to 0.06 Gm. (¾ to 1 grain) for fifteen months, without untoward effects. For our part, we have utilized the various animal preparations in a systematic manner and for extended periods, and have been led to the conclusion that they are entirely ineffective.

In view of these unsuccessful efforts on the part of medicine, the surgeons, emboldened by the increasing safety attending their operations, were not afraid to attempt the **removal of the hypophysis.** The anatomical situation of the gland seemed to make the access



Opening the sphenoidal sinus, of which the median cell is visible. (*R. Proust.*)

to it well-nigh impossible. Nevertheless, encouraged by the results obtained by physiologists, and having gained additional information and on November 16, 1907, Schlosser performed the operation of removing a tumor of the hypophysis from a living person.

Trephining the posterior wall of the sinus. The pituitary, marked with a white cross, can be seen in its dorsal sheath. (*R. Proust.*)

through researches on the cadaver, the operators ascertained the avenues of entrance which would permit of their reaching the pituitary gland,

In theory, the hypophysis may be reached, according to Toupet, either by an intracranial or by an extracranial route. Those who favor the intracranial

method advance as their chief argument the less danger of infection to which the patient is subjected, and propose either the frontal route (Krause, Kiliani) or the temporal route, already employed in their experiments by Caselli and Horsley (Brit. Med. Jour., Aug. 25, 1906). The supporters of the extracranial route are the more numerous at the present time. Against the former method they raise the objections of operative difficulty, severity of operative interference, and the great ease with which a communication may accidentally be established between the cavity of the sella turcica and the sphenoid sinus, of which the thin and fissured walls, in the presence of tumor of the hypophysis, may yield to the slightest touch. According to these observers, the possibility of such a communication would greatly reduce the chances of performing an aseptic operation by the intracranial route. Moreover, the extracranial operation induces but a minimal degree of shock, and is comparatively easy in technique; it does not, however, exclude the chances of infection.

> The intracranial method is dangerous, uncertain, and difficult, while the oral route gives but a limited operative field and is almost sure to be followed by infection owing to connection with mouth. Hecht (Jour. of Nerv. and Ment. Dis., Nov., 1909).

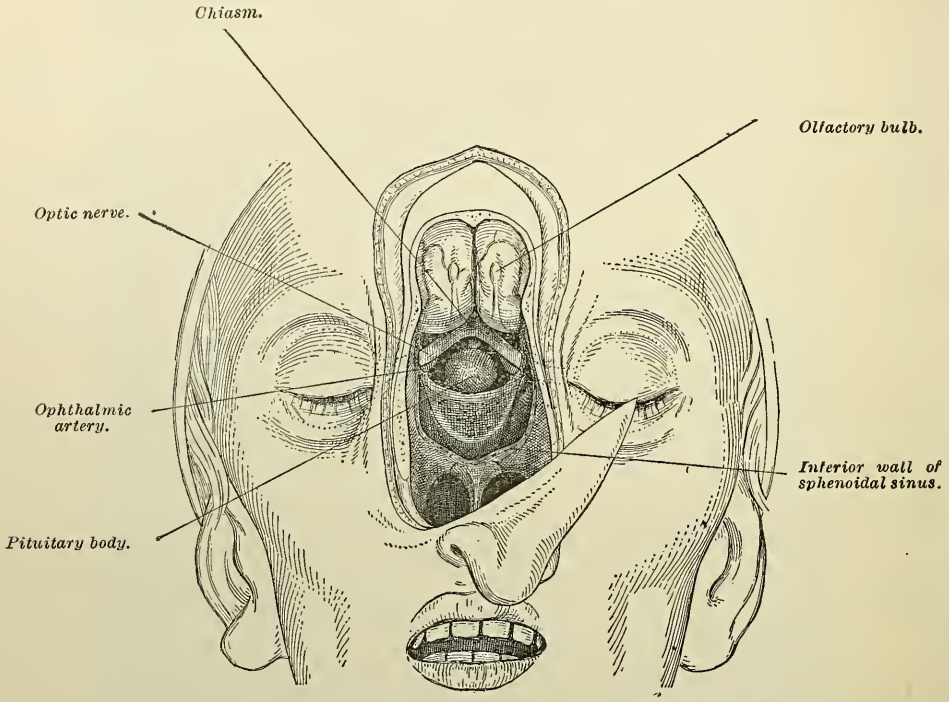
We cannot here enter into detail concerning all the proposed technical methods of reaching the sella turcica through the sphenoid sinus. According to their respective temperaments, surgeons have planned either sweeping and broadly mutilating operative procedures or else more economical methods. These procedures may, in their main features, be reduced to four, as follows: 1. The simple nasal route, practically the only one which has been employed in man. 2. The nasal route combined with more or less extensive resections of the superior maxilla and the inner wall of the orbit, even to sacrificing completely an eye already functionally lost (Schlosser). 3. The buccal route of Gussenbaum, with resection of the hard palate, advocated by König (Berliner klin. Wochenschr., No. 46, p. 1040, 1900). 4. Transverse and median suprahyoid pharyngotomy, proposed by Loewe (*ibid.*, Feb. 17, p. 378, and Feb. 24, p. 422, 1908).

Of all these methods, the simple nasal route is the one which has been used almost exclusively, with slight variations in technique, on the living subject. Horsley and McArthur alone seem to have employed the temporal intracranial route.

With the omission of a few details, the operative technique may be summarized as follows: Temporary resection of the nose, which is reflected laterally above and below; resection, osteoplastic if desired, of the anterior wall of the frontal sinus; excision of the vomer and of the nasal septum to its insertion posteriorly, which is preserved as a landmark, showing the median line; removal of all the ethmoid air-cells and of the turbinated bones, to permit of seeing and opening into the sphenoid sinus. The sinus having been entered, the next step is to make an opening at the bottom of the sella turcica, the anterior wall of which bulges forward. The dura mater is then incised. The tumor is removed piecemeal by means of the curette. (The tumors hitherto removed have generally been very soft, sometimes cystic, as in Eiselsberg's case, and their excision presented no difficulty.) The cavity of the sella turcica is then drained by means of a rubber

tube which passes out through the nasal fossæ; the latter are packed, and, as a final step, the nose, temporarily drawn aside, is put back in place.

This operation is accompanied by marked bloody oozing, which yields rapidly, however, to packing with adrenalin solution in 1 : 1000 strength, and generally ceases at the end of fifteen minutes.



Relations of pituitary body, as exhibited in the nasal route of operative access, with additional removal of bony floor of anterior cerebral fossa. (*Proust.*)

Successful cases of hypophysectomy are of interest not only from the standpoint of the treatment of acromegaly, but also from that of its pathogenesis. With respect to the latter, they possess the same value as true experimental studies, and it will be worth while here to give a *résumé* of the first two cases operated by Hochenegg.

The first patient, presented before the German Congress of Surgery in 1908, and whose history was later reported *in extenso* by Stumm, was a young lady, 31 years of age, in whom the initial dystrophic manifestations had appeared at about the 25th year and soon become fully developed. The operation was indicated because of the severity of her headache and visual disturbances. It was carried out by the nasal route. No untoward after-effects appeared, and immediate results were obtained. Upon awakening the subject was already relieved of the intolerable headaches which had made her life miserable. Vision rapidly improved. A more remarkable event was further witnessed in that, on the fifth day, the symptoms of acromegaly began to disappear. The patient regained the ability to close her mouth completely, which she had been unable to do before. Her tongue and

nose soon after began to decrease in size. A similar change was observed in her feet and hands: their diminution in bulk was so marked that, on leaving the hospital, she was obliged to wear three pairs of stockings in order to make use of her shoes, and that her fingers and wrists literally floated around in the gloves she had worn before the operation. The change in her appearance was such that her family had difficulty in recognizing her. We may add that her menstruation, long since arrested, resumed its usual regular course, and that in August, 1908, a parenchymatous goiter appeared in her neck.

The second case operated by Hochenegg appeared as though modeled after the first. The patient was a woman of 34, in whom the disease, dating back ten years, had produced the most typical dystrophic changes, and was associated with amenorrhea, headache, and disordered vision. Excessive hairy growth and alterations in her voice gave her a peculiar masculinity. The operation was carried out with the same technique as before and was likewise crowned with success. At the end of a week the headache had almost completely disappeared. The extremities diminished in size to such an extent that three months after the operation, when Exner presented the patient before the Medical Society of Vienna, the third toe measured ¾ cm. less in circumference, and the middle finger ½ cm. While the menstrual periods did not reappear, the hairy appendages resumed their normal state, and, as in the first patient, the thyroid gland increased in volume; a growth the size of a walnut developed from the isthmus.

Different measures should be adopted under different circumstances: (1) comparatively small tumors in the sella turcica covered with a tent of dura mater can be removed completely by the nasal route; (2) growths growing endocranially, but filling the sella turcica, can be removed in part to relieve the pressure symptoms, though not the acromegaly; (3) endocranial growths, removal of which can only prove harmful. Hochenegg (Deut. Zeit. f. Chir., Bd. c, S. 317, 1909).

Confirmation of Paulesco's observation that simple division of the stalk of the pituitary is as fatal a procedure as removal of the latter organ also, and also of the view that the latter procedure in animals is invariably followed by death within a few days. This fatal result is evidently due to removal of anterior or epithelial lobe, since removal of the posterior or neural lobe is followed by no characteristic symptom. Cushing and Redford (Johns Hopkins Hosp. Bull., April, 1909).

Removal of part of the pituitary for the relief of acromegaly by the transsphenoidal route. The patient was a typical case of acromegaly, with partial blindness and epileptic crises. A tumor of the hypophysis was diagnosticated, and operation was done by opening the nose, passing through ethmoidal and sphenoidal cells into the sella turcica, and the removal of a considerable amount of tissue from the hypophysis. The patient lived some six weeks after the operation, the external wounds entirely healed, but he died suddenly. An examination of the skull and brain after death showed that the tumor of the hypophysis was an epithelioma with several prolongations into other parts of the skull and around the cavernous sinus. It was entirely unencapsulated, and could not have been removed by the route taken or any other. Lecene (La Presse médicale, Oct. 23, 1909).

The writer performed the following operation on the cadaver: An incision is made from the frenulum of the upper lip to the last tooth through the mucous membrane and periosteum down upon the facial wall of the antrum of Highmore, which is laid bare and then removed. The mucous membrane of

the antrum is then removed, a portion of the medial wall chiseled away, the sphenoidal sinus entered and removed as thoroughly as possible with chisel, forceps, and sharp spoon. The posterior part of the septum is then removed with a few blows of the chisel, the sphenoidal rostrum cut through, and the septum between the cavities removed. This leaves the bone beneath the hypophysis exposed and ready to be cut through with the chisel. Fein (Wiener klin. Woch., July 14, 1910).

McArthur has operated by a lateral route, advancing to the middle along the roof of the orbit and in the one instance was able to remove about two-thirds of the growth. The author believes that the nasal route is the best, despite the resulting deformity. He reports on 6 cases of tumor of the pituitary. Case I was diagnosed from the menstrual history, double temporal hemianopsia, optic atrophy, and the X-ray picture, but no operation was performed. Case II, a boy of 14, had no evidence of acromegaly. Headache came on at intervals since the third year, with vomiting, frequently terminating in nosebleed, with apparent relief. Double optic atrophy with hemianopsia showed a pituitary cyst with calcareous plates. This case was operated by Horsley, and a pituitary cyst containing chocolate-like fluid was evacuated. The convalescence was satisfactory, but the boy died eighteen months after the operation. Case III, a woman of 25 years, ceased to menstruate at 22, had headaches, bilateral nasal atrophy, and diminution of the eye-grounds. An X-ray showed a much enlarged sella turcica. At operation, going over the orbital plates, a cyst of the pituitary was reached and evacuated, but the frontal lobe was lacerated in the procedure, and the patient died in eighteen hours. Case IV, a man of 36 years, had for five months noticed the eyesight of left eye failing, and he had intense left-sided headaches, which became less in the last two months. The field of vision showed a sharply defined, right-sided, temporal hemianopsia. The patient had been impotent for a year. An X-ray showed an enlarged sella turcica. He was operated by von Eiselsberg by the nasal route, and recovered. The tumor was a malignant epithelioma. Case V, a boy aged 14, for one year had noticed his vision getting bad, and later there were temporal headaches; later hemianopsia was found and atrophy of the disk. The X-ray showed an enlarged sella. Though operation was refused, the boy lived over four years after the symptoms of tumor were felt. Case VI, a man of 33, had for six years noticed failing vision in one eye, and later of the other, the outer half of the field going first; marked atrophy of the disk on one side. The X-ray showed a large sella turcica. No operation was performed, because the patient was in such excellent good health, with no other symptoms than those of the eyes. Church (Jour. Amer. Med. Assoc., July 10, 1909; Interstate Med. Jour., Feb., 1910).

The author is inclined to think that cases of the Marie type, with hyperplasia or the adenomatous condition, represent hyperpituitarism, and that cases of the Fröhlich group represent hypopituitarism in consequence of invasion of compression of the gland by a tumor or cyst.

The case reported was one of acromegaly in a man of 38. Constant headache and photophobia were prominent symptoms, and these were practically cured by partial hypophysectomy—which was followed, also, by marked reduction in the thickening of the fingers, tongue, and jaw.

For this operation temporary tracheotomy was first performed. In Rose's position an omega flap was made over the frontal sinuses, continued down on each side of the nose to the base of the nasal bones. An osteoplastic flap was then turned down. An opening was made in each frontal sinus, and these were joined by a Gigli saw; with forceps the lateral incisions of the proposed frontonasal flap were carried down through the nasal bones; the median septa were divided with chisel. The ethmoidal cells were rongeured

away to provide a channel 2 cm. wide, below the ethmoidal roof, to the posterior part of the nasal fossa. The sphenoidal cells were then broken into, the projecting sella turcica exposed and chiseled away. The dura enveloping the pituitary gland was thus exposed. It was incised, and about one-half of the exposed portion of the gland was removed, piecemeal, by curette. Two cigarette drains were introduced into the sphenoidal cells, one emerging from each nostril. The frontonasal flap was then sutured in place. Primary union.

In addition to tracheotomy, plugging of the posterior nares and swabbing the nares with adrenalin preceded the operation. Urotropin administered for twenty-four hours before operation. Anesthesia by warmed ether vapor.

In dogs the hypophysis is easily exposed by the lateral cranial route, bilateral craniectomy being performed to allow dislocation of the brain (Paulesco). In man the exposure by this route is hazardous, if not impossible, and Horsley's approach (temporal intracranial) seems to be eligible only for a growth lying well above the sella turcica. The transsphenoidal operations are those of choice for growths within the sella turcica, as first advocated by Schloffer, and of these the writer regards as best a direct median approach through the nose (extracranial). Harvey Cushing (Annals of Surg., Dec., 1909; Amer. Jour. of Surg., March, 1910).

From this brief discussion of the surgical aspect of acromegaly we may conclude that hypophysectomy is practicable in the human subject by the nasal route, and that it represents a relatively safe operation. Surgical intervention has yielded results which could not have been hoped for from any mode of treatment previously employed.

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AND
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Paris.

ACTINOMYCOSIS.—DEFINITION.—A parasitic, infectious, and inoculable disease due to the development of the actinomyces, or ray fungus. First described in 1877 in cattle by Böllinger and in man by James Israel; it can no longer be considered a rare disease. From its frequent development in the lungs it has often been confused with tuberculosis.

SYMPTOMS.—The symptoms vary according to the locality of the disease. The affection is chronic and exceptionally rapid. The granulation tissue is abundant and the mass resembles a tumor. Previous to suppuration it is quite firm, and, if progressing rapidly, is surrounded by diffuse edema. Pain and tenderness hardly ever exist. When suppuration occurs the mass increases rapidly in size.

Actinomycosis may develop in almost any part of the body, but Poncet and Bérard showed, after an investigation of 500 reported cases, that the sites of predilection were relatively as follows: Head and neck, 55 per cent.; thorax and lungs, 20 per cent.; abdomen, 20 per cent.; other parts, 5 per cent. In France the face and neck were affected in 85 per cent. of the 66 cases reported.

1. Cutaneous Surface.—Usually, a lesion of the skin is secondary to the evolution of an underlying actinomycotic tumor, which, by its growth, bursts through the skin. A sanguineous or purulent liquid, containing the characteristic grains, issues from the ulcerations so formed. The grains are small, opaque, yellowish-white, or yellowish masses about as large as a pinhead, which are composed of smaller grains, measuring about $\frac{1}{10}$ mm. These smaller grains are formed by a central mass, of interwoven or straight fibers, whence extend toward the periphery spoke-like

prolongations, with club-like terminations. Rarely the affection may develop primarily on the fingers, hand, nose, or face. It forms a small, round, ligneous mass, which may soften in a few weeks, burst through the skin, and give a granulous and varied pus, containing actinomycotic granulations. The border of the granulation is uneven, violet-hued, and undermined. Around the original mass there arise secondary masses; so that the entire lesion forms a violet-red, indurated patch, deeply adherent, and somewhat resembling scrofuloderma.

In cutaneous actinomycosis the lymphatic ganglia are usually not enlarged. Pain is, in some cases, intense; in other cases it is awakened only by pressure. The pathognomonic spots, which are more or less deep in color, according as the general color of the lesion is more or less pronounced. If the general color is pale, the spots are bluish red or violet; if the tint of the mass is deeper, the spots present a blackish or slate color. These spots vary in size from that of a pea to that of a pin's head. They appear to correspond to the points at which the wall of the abscess is thinnest, and it is here alone that fistulæ form.

In some instances, as in the case reported by Pringle and illustrated in the annexed colored plate, the lesions may assume the appearance of large sarcomatous-looking growths, ulcerating at various points, situated upon hard, brawny, and deeply undermined skin and from the ulcerative points of which pus exudes, mixed with characteristic yellow granules, actinomycosis.

2. Alimentary Canal.—*Teeth.*—The fungus has been found in carious teeth (Israel), often side by side with leptothrix (Senn), or almost pure culture with no manifestation of disease except chronic periodontitis (Partsch). Carious teeth have increasingly been shown to be the origin of the affection.

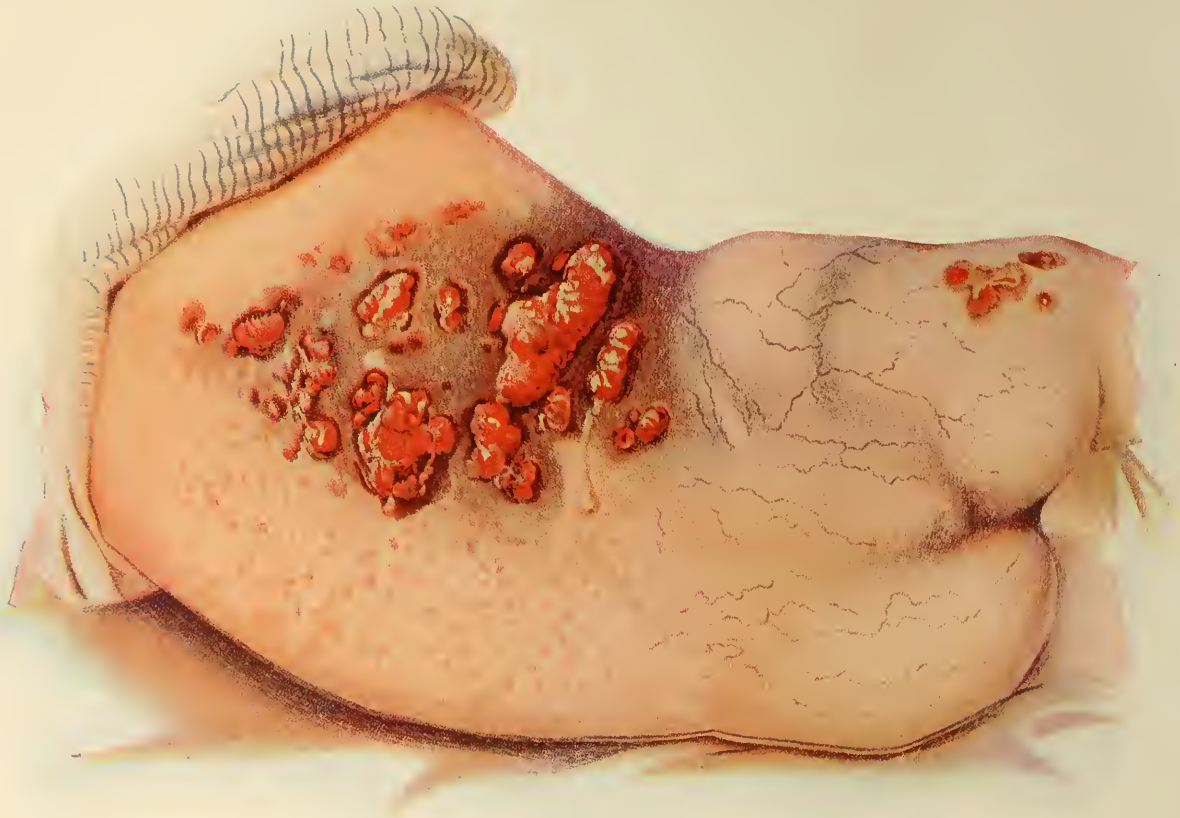
Tongue and Tonsils.—In man three cases of this affection have been found on the tongue, one of which was of primary development; the other two are believed to have found origin in a carious tooth. The tonsils may also be affected and be the seat of white projections resembling masses of moss, which seemed to grow in the crypts. The pharyngeal wall also shows these white masses, as a rule.

Lingual actinomycosis in cattle appears as a nodular tumor, with prolongations into the parenchyma, of ligneous hardness.

Jaws.—The lower jaw is the most frequently affected. At first the disease resembles periosteal sarcoma, until the loose tissues of the neck are reached, when it often rapidly extends downward along the subcutaneous connective tissues and intermuscular septa. According to Poncet, an early sign of actinomycosis in this location, in some cases, is a marked difficulty in opening the mouth, long before the presence of the disease can be determined microscopically.

> Eight cases tending to show that a proportion of the cases ranking as alveolar abscesses may be due to the specific organism of actinomycosis. Few cases enter hospital with advanced actinomycosis of the jaw, and many recover after simple incision and after rupture. Certain cases of generalized disease in the lungs, intestinal tract, liver, etc., occur in which the organism gained entrance through the food, or was swallowed, and therefore the surgeon should aim at making external drainage. C. A. Porter (Boston Med. and Surg. Jour., Sept. 13, 1900).

The upper jaw is rarely primarily affected. It then tends to attack rapidly



Case of Actinomycosis Extensively Involving the Skin. (*Pringle.*)

Transactions of the Royal Medico-Chirurgical Society.

the adjacent parts, and even the base of the skull and brain.

Autopsy indicating that actinomycosis of the middle ear may arise from blood-infection from a primary focus elsewhere in the body, or from a neighboring actinomycotic process in the mouth, pharynx, tonsil, or from carious teeth; that the fungus may enter the middle ear through the Eustachian tube or through the external auditory canal. J. C. Beek (Prager med. Woch., Mar. 29, 1900).

In three cases the predominant sign was a sharply defined local movable mass, which is always strongly indicative of the disease. Hofmeister (Beit. z. klin. Chir., B. 26, H. 2, 1900).

In the case of a butcher the first signs were in the floor of the mouth, in the form of a pseudoranula; afterward swelling of the cheek showed characteristic yellowish discharge and granules. Lenoir and Claisse (Jour. des Praticiens, July 14, 1900).

3. Intestinal Canal.—The disease begins with a sharp, lancinating pain in the abdomen and follows the course of chronic peritonitis. Swellings forming abscesses are found on the anterior abdominal wall, which sometimes communicate with the intestine. It may also start from the vermiform appendix. There have also been cases of primary actinomycosis of the colon with metastatic deposits in the liver.

Actinomycosis of the vermiform appendix was first recognized by Barth in 1890, and was first recognized in England in 1892 by Ransom. It has become evident, however, that a number of cases really originate in the cecum, and an identical clinical picture may result after perforation. Hence a preferable title would be "actinomycotic perityphlitis." Three cases observed by the writer in one year, and he describes three more from the annals of the Bristol Royal Infirmary. Grill mentions 77 cases of actinomycotic perityphlitis as recorded up to 1895. It is probable that the total number up to 1904 is about 150, of which 27 are English. The proportion as to the sexes is about 5 males to 2 females. It is more frequently seen between 20 and 30 years of age. A large number of sufferers are connected in some way with farm life, or deal with corn. Short (Lancet, Sept. 14, 1907).

4. Genitourinary Tract.—The uterus may also become invaded by the disease, the first manifestation being the discharge of a turbid, fetid fluid containing the characteristic shreds and masses.

Case of a peasant woman in which the labium majus was swollen and covered with orifices of fistulæ discharging pus. The tracts were slit up freely and scraped; the actinomyces was detected by aid of the microscope. Three-quarters of a year later no signs of recurrence could be detected. Only two similar cases have been recorded, one by the writer himself, and one by Lieblein, of Prague. Bongartz (Monats. f. Geb. u. Gyn., Nov., 1902).

Up to the present only one case (von Israel) of the primary renal actinomycosis has been published. The writer reports a second case, which occurred in a boy, aged 4¾ years, who, like von Israel's patient, was operated on with successful result. Kunith (Deut. Zeit. f. Chir., Bd. xcii, S. 181, 1908).

The gross macroscopic and microscopic picture resembles that of tuberculosis in many cases. Bollinger's desideratum for the diagnosis of actinomycosis, namely, that corpora flava must be present, is untenable at the present time. Repeated bacteriological examinations, and sometimes long and tedious ones, of the same specimens must be made to insure a correct interpretation of suspicious pathological material. Inoculation with pure cultures into the animal is not attended with success. Only the injection of pus with actinomycosis, or the ingestion of material

upon which actinomycosis is grown, will prove successful in the production of actinomycosis in the animal. Actinomycosis does not travel by the lymphatics, and probably not by the blood route. The prognosis is favorable in circumscribed cases, which is most likely the condition in which we find the uterine appendages.

The treatment consists in radical extirpation and free drainage, the application of tribromphenolbismuth, or irrigation of the fistula with copper sulphate. The internal administration of large doses of iodide of potash up to 75 grains a day, which exerts a positive healing effect. Carl Wagner (Surg., Gynec. and Obstet., Feb., 1910).

5. Respiratory Tract.—In bronchitic actinomycosis the affection is less severe in winter than in summer, which is the contrary of what is observed in ordinary bronchitis. It can be classified in three groups: (1) lesions of chronic bronchitis; (2) miliary actinomycosis, and (3) cases with bronchopneumonia and abscesses. The lower lobe is attacked more frequently than the upper; the opposite is the case in tuberculosis.

Review of 14 recorded cases of actinomycosis of the lung. The only 2 which recovered were those in which radical operations, with resection of four or five ribs, and cauterization of the diseased cavity in the lung were carried out. All those that were simply incised and drained ended fatally. The infection of the lung may be secondary to either cervicofacial or pharyngoesophageal actinomycosis, or it may be primary, either through the bronchi or from an external wound. There are three forms clinically: (1) the pulmonary, with insidious onset, going on to induration of a large area of lung, generally in the subclavicular or posterolateral regions, the apices being usually free; (2) the bronchial, with a diffuse catarrh and fetid mucopurulent expectoration, containing the fungus; (3) the pleural, with effusion; the coexistence of pleural effusion with retraction of some part of the thoracic parietes—due to fibrous changes in the lung—is pathognomonic. Another pathognomonic symptom is the presence of a swelling in the wall of the thorax where it has been invaded by the fungus, along with shrinking of the lung, causing retraction of the thoracic walls; later on this softens and becomes subfluctuating without the formation of large abscesses. Puncture obtains a fluid containing fragments of fungus. Death may occur after months or years, according to the varying invasion of other organs by the disease; in one case of rapid diffusion of the fungus death occurred in twenty-four days. Parascandolo (Brit. Med. Jour., from Clinica Mod., Nov. 7, 1900).

Mammary actinomycosis may occur in two ways: primary and secondary. In the former infection occurs either from propagation of the actinomycotic grains in the milk-ducts or from their penetration into the tissues through a continuity of the skin. Four cases of the primary form witnessed. The secondary form spreads to the mammæ from the lung (most frequently) or some other organ. The disease is not easy of diagnosis, and is liable to be confused with tubercle, cancer, interstitial inflammation, or syphilitic disease, and repeated microscopical examination of discharges or pieces of tissue should be made. The prognosis in the primary form is good, but in the secondary form unfavorable. Mileff (Gaz. d. Hôp., Jan. 1, 1901).

The diagnosis of "primary pulmonary actinomycosis," even in the absence of all abdominal symptoms, must remain doubtful without a postmortem examination. In abdominal, as well as in pulmonary, actinomycosis the patient should be closely questioned regarding any previous more or less indistinct symptoms of appendicitis and sores at the anus. Fecal concrements found in the appendix in cases of actinomycosis should be microscopically examined. In actinomycosis following typhoid-

like symptoms, a Widal test should be made. At the post-mortem special attention must be paid to intestinal scars, which may easily avoid detection. Experiments and clinical observation indicate that the fungus cannot enter the human or animal body without a wounded surface. Must the wounded body also be the carrier of the infectious material, or can infection take place secondarily through a granulating accidental wound or the chronic ulcers described? Human actinomycosis of the skin, or actinomycosis of the jaw in pasturing cattle, may offer a suitable object for investigation in regard to the latter point. Fritz Maas (Annals of Surg., Aug., 1903).

Case of intralaryngeal actinomycosis. The patient, aged 19, first noticed a slight hoarseness, which gradually increased until he could speak only in a whisper; it was for this symptom alone that he sought relief. There was at times a slight "stinging" in the throat, which had never been more than disagreeable. There had been a slight cough and some dyspnea on exertion. In the region of both true cords and completely covering and concealing them were irregular masses of dirty-white tissue, more than half occluding the chink of the glottis. The same sort of tissue lined the trachea as far down as the writer could see, which was but a short distance, by reason of the encroachment on its lumen by this adventitious material. The man was given vigorous antisyphilitic treatment for a month, without improvement. After he had been under observation for about three months, several portions of the laryngeal mass were removed and examined microscopically. The diagnosis of actinomycosis was then made. The patient was put on increasing doses of potassium iodide without apparent improvement, although there soon was no evidence of actinomycosis in the sputum. There were present occasional tubercle bacilli, streptococci, and groups of staphylococci. This condition gradually became worse. Physical signs of consolidation were discoverable in the right upper lobe. There were some cough, emaciation, irregularity of temperature, anorexia, and digestive derangement. At the last examination there was an area in the vault of the pharynx which presented an appearance identical with that in the larynx—previously there had been absolutely no lesion discoverable elsewhere than within the larynx. The physical signs then present were the classical ones of early pulmonary tuberculosis. Arrowsmith (Laryngoscope, Oct., 1910).

Actinomycosis of the lungs is found in 20 to 30 per cent. of all cases of actinomycosis. It probably originates in the mouth, and usually takes the form of bronchitis or bronchopneumonia. The diagnosis is made by finding the "sulphur granules" in the sputum, and the streptothrix under the microscope. J. O. Alksne (Deut. Aerzte Zeit., Mar. 15, 1910).

6. Brain.—Here, tumor-like symptoms exist during life, with headache, paralysis of the abducens, congestion of the optic papilla, and attacks of unconsciousness. In a case reported by Ranson the autopsy indicated the probable mode of infection of the orbit and brain. A sinus was found leading from the orbit to the gum of the upper jaw; the ray fungus had probably lodged in or near a tooth, as it has so often been found to do. The fungus was probably carried into the system on an ear of corn chewed at harvesttime. Having reached the orbit, it crept along its outer wall and in the wall of the right cavernous sinus to the base of the brain, ultimately setting up meningitis and small abscesses, and burrowing through the pituitary body and sella turcica to the cavernous sinus of the left side.

The orbit is very seldom the seat of actinomycosis. A case is reported from von Brun's clinic, and 9 cases

are cited in detail from the literature. The author's case was the first to be operated upon by temporary resection of the upper part of the cheek-bone, a procedure which is considered superior to Krönlein's resection of the lateral portion of the orbit. The chief symptoms were exophthalmos and failure of vision in the affected eye. There was also lack of mobility of the eyeball. These symptoms are, however, not pathognomonic of actinomycosis, it being essential to an exact diagnosis that the ray fungus be found in the pus. As soon as a diagnosis is made, or there is a well-grounded suspicion of this disease, steps should be taken to radically remove the focus of infection. Müller (Beiträge z. klin. Chir., Bd. 68, H. 1, 1910).

DIAGNOSIS.—When the process is very rapid, actinomycosis may stimulate acute phlegmonous inflammation and osteomyelitis, or, when widespread, syphilis.

A study of all cases reported showed that the clinical characteristics vary greatly with the region of the body involved. In the cervicofacial and cutaneous, as well as in many of the thoracic and abdominal, cases the first symptoms noticed were pain and swelling, though the pain was not often severe and may be absent entirely. Fever above 101° F. is rare, and examination of the blood shows a leucocytosis, averaging 17,000. Injections of tuberculin failed to give a febrile reaction. Cervicofacial cases are often mistaken at first for toothache; in thoracic forms the first symptoms are those of bronchitis or pleurisy, and abdominal cases often resemble appendicitis. The diagnosis should never be positive without finding of the organisms which occur in the sulphur granules of the abscess contents. Although the progress of the disease is sluggish, extension is prone to follow by direct involvement of the contiguous tissues or by metastases. W. G. Erving (Bull. Johns Hopkins Hosp., Nov., 1902).

Sarcoma.—This form of neoplasm does not suppurate or break down so early.

In the jaws it is to be differentiated from dental affections: epulis.

Tuberculosis.—In this disease the lymphatic glands are infected, and the apices are usually the first involved.

Carcinoma.—The skin or mucous membrane involved is in close connection with the tumor; in actinomycosis the skin will be found broken on microscopical examination.

Case of a farmer suffering from actinomycosis of the jaw. After the disease existed for upward of a year, a surgeon diagnosed it as cancer, and advised removal of the right half of the lower maxilla. Three months later this patient was exposed to the X-ray treatment for three months, twenty-five applications of the light being made in that time. The treatment was perfectly futile. After three months' rest the patient consulted a second X-ray specialist, who gave twenty applications in nine weeks with negative results. Iodine treatment, begun two years from the beginning of his trouble, was, however, followed by a marked improvement. Heidingsfeld (Cincinnati Lancet-Clinic, Mar. 28, 1903).

Many actinomycotic tumors have been removed surgically under the impression that they were due to cancer, and a cure of the latter hailed in consequence of their non-recurrence. Mercury and the iodides will cure actinomycosis, which is thus often mistaken for syphilis to the normal detriment of the patient; the iodide treatment, however, is counseled in all doubtful cases. Poncet and Berard (Lyon Méd., Mar. 27, 1904).

Syphilis.—A gumma will, in two or three weeks, be sensibly affected by large doses of potassium iodide, which does not act so rapidly in actinomycosis.

The undoubted influence exercised by iodide of potassium countenances

the suspicion that many patients supposed to be syphilitic have really been actinomycotic. Poncet (Glasgow Med. Jour., April, 1895).

Lupus.—The diagnosis depends, in this condition, upon microscopical examination.

Ten cases which simulated actinomycosis, but in which the causal agent was either the *Cladothrix liquefaciens* or the bacillus described by Sawtschenko. Radical removal of the focus is the only treatment. G. Kleseritzky and L. Bornhaupt (Archiv f. klin. Chir., Bd. lxxvi, Nu. 4, 1905).

Case of actinomycosis of the big toe, in which there was marked resemblance of the pathological and microscopical picture to Madura foot. The patient had had inflammation of the big toe, with suppuration of the matrix of the nail, followed some months after its complete subsidence by another thickening of the toe, but without any pain or other disturbance. Two years after the shedding of the nail the toe rapidly increased to the triple circumference of the opposite toe, vesicles appearing on the skin and undergoing suppuration. The toe was amputated, and the examination showed the presence of actinomycosis. Kulbs (Wiener klin. Woch., Nu. 2, 1907).

The writer was able to differentiate actinomycosis by the seroreaction in 8 cases, the only negative reaction being in a case in which the cure had been complete for over four years. The specific reaction is both by agglutination and by fixation of complement by means of the spores of the sporotrichum. Actinomyces cultures cannot be used for the tests, but the generic reaction with sporothrix spores is constant and lively. It is specific for actinomycosis, sporotrichosis, and thrush, but these can be readily distinguished. Widal (Bull. de l'Acad. de Méd., May 10, 1910).

ETIOLOGY.—Both men and animals are probably infected from vegetables or water (Israel), from eating ears of barley, or rye, when the fungus penetrates through the wound or abrasion thus provoked, or in many cases through carious teeth. Intestinal actinomycosis is due to taking contaminated food or water, when the fungus becomes implanted upon an already diseased tissue, multiplies, and causes active proliferation of the submucous tissue. It may be transmitted by kissing, as in a case reported by Baracz. Farmers should be warned against the habit, so common among them, in chewing bits of straw, wheat, oat-chass, etc., the most prolific cause of the disease. Actinomycosis is frequently met with in shoemakers. This is due to their habit of placing their needles in their mouths (Ullmann).

Actinomycosis of the lower jaw acquired by a toothbrush-maker in the following manner: Hogs' bristles were washed, then held in mouth before sticking into the handle-holes in bundles. Guinard (Bull. et Mém. de la Soc. de Chir. de Paris, T. 26, No. 6, 1900).

Total of 72 cases of actinomycosis from American sources collected. Six personal cases, 2 of which had not been previously reported. In one, alveolar abscess followed chewing wheat-grains with a carious tooth. In a second case a quantity of pus collected in the right iliac fossa. The patient died of malnutrition, having recurred after evacuation. J. Rührah (Annals of Surg., Feb., 1900).

All the reported cases of actinomycosis in man carefully studied. The cases are scattered widely throughout the country, though most are reported from large medical centers. Less than 20 per cent. come from the Southern States. Males were affected about three times as often as females. The youngest case reported was a child 6 years old; the oldest a man of 70; most are in middle life. Con-

cerning occupation, there is a wide range, but 36 per cent. had much to do with live stock and grain. The chronic character of the disease was well shown by the fact that in 62 per cent. it lasted over six months. W. G. Erving (Bull. Johns Hopkins Hosp., Nov., 1902).

Large number of cases collected in which actinomycosis which had remained latent throughout pregnancy suddenly took on a very rapid development as soon as this was ended. The curative action of iodine on the disease and the frequent disturbance of iodine metabolism in pregnancy and the puerperium may have something to do with this relation. Thevenot (Revue de Chir., No. 9, 1906).

Primary invasion of the skin and subcutaneous tissues by *Actinomyces bovis* is of rare occurrence. The cases number less than 20. Even some of these may have been due to secondary rather than primary invasion of the skin. Personal case of actinomycosis of the skin of the foot. Leser was the first to arouse interest in this particular localization by the publication of 3 cases. Leo Buerger (Amer. Jour. Med. Sci., Nov., 1907).

In the case reported a scrap of a head of barley was found sticking in the tissue of the sublingual gland, the outer end in one of its excretory ducts. Söderlund (Upsal a Läkare, Förhandlingar, vol. xiv, Nos. 3-4, 1909).

Only 6 cases for actinomycosis of the ovary are on record, and none of these are primary. Case of the latter kind in a patient who had lived in London for 16 years, but in 1903 and 1904 was brought into contact with hay, straw, and corn, the usual sources of actinomycosis, and it is noteworthy that the symptoms date from 1904. As there was no evidence of disease in any adjacent organ, the streptothrix must have reached the ovary by way of the blood-stream, the mode of entry into the body being, the authors suggest, some crytogenic focus—*e.g.*, the tonsil, through which, it is well known, micro-organisms may pass into the blood-stream without producing any local lesion. Taylor and Fisher (Lancet., Mar. 13, 1909).

The writer has observed a number of cases in which latent actinomycosis was roused to active proliferation by some intercurrent trauma. He has also found similar instances in the literature. There may be an interval of years between the trauma and the manifest actinomycotic process; in one case seventeen and in another ten years had elapsed, and intervals of five and ten years are by no means uncommon. Noesske (Med. Klinik, Mar. 27, 1910).

PATHOLOGY.—The actinomycoses were formerly thought to be mold fungi (hyphomycetes), but Bostroem, in 1885, proved by cultivating them that they were a variety of cladothrix, belonging to the schizomycetes.

Comprehensive study on the biology of the branching filamentous micro-organisms isolated in pure culture from 13 cases in man and 2 in cattle of actinomycosis. The writer considers the organisms to be all of one species, essentially an anaërobe, growing well only in agar and bouillon and in the incubator. He found that the filaments took on the "club" appearance only when grown in immediate contact with animal fluids or within the animal body. Experimental inoculation caused the formation of tumor masses of small sizes, which showed but little progressive tendency. The organism could be regained, but there was little evidence that multiplication had taken place within the animal.

The writer considers *Actinomycosis bovis* to be the proper name for the organism. He does not accept the prevalent belief, based on the work of Bostroem, Gasperini, and others, that the specific infectious agent of actinomycosis is to be found among certain branching micro-organisms widely disseminated in the outer

world, which differ profoundly from *Actinomycosis bovis* in having spore-like reproductive elements. On account of the fact that the organism he describes does not grow on all culture media, and practically not at all at room temperature, he does not believe that it has its usual habitat outside of the body. The organism is a normal inhabitant of the secretions of the buccal cavity and of the gastrointestinal tract. The part played by foreign bodies is in the formation of a nidus where the actinomycoses develop to form actinomycosis, and he does not think that straw and like foreign bodies so frequently found in actinomycotic lesions are the carriers of the micro-organism.

The "club" formation about the filaments is a protective function. The bacteria so frequently found accompanying the disease are important in the spread and continuance of the infection, forming new sinuses, to be reinfected with *Actinomycosis bovis* from the alimentary canal. J. H. Wright (Jour. of Med. Research, vol. xiii, p. 349, 1905).

The mass is made up of granulation tissue, which, except for the presence of the ray fungus, would be mistaken for a round-celled sarcoma. Epithelioid elements and giant cells are also seen. In the granular mass, or in the pus coming from a case of actinomycosis, the fungus itself appears under the form of small, yellow, brown, or even green masses, about a pinhead in size, which, on microscopical examination, are found to be composed of a central interwoven mass of threads, from which radiate club-shape-ended rays; in some specimens certain rays project far beyond the others. In man the clubbed bodies are frequently absent (Senn). The histological lesions are alike in the actinomycotic nodule and in the tuberculous follicle; only the foreign body differs. Water or a weak solution of sodium chloride causes the rays to swell enormously and lose their shape; ether and chloroform have no action upon them.

The yellow grains are not always to be found in fistulæ, etc., unless they are carefully sought in scrapings, etc. An early diagnosis is essential, since later the disease may be beyond the resources of therapy. A. Poncet and L. Bérard (Le Bull. Méd., Mar. 28, 1900).

Case in which microscopically there was no appearance of the ray fungus in the fresh pus, and yet microscopical examination showed the presence of fungus at once. The absence of the typical grouping of the micro-organisms is not sufficient to exclude the diagnosis of actinomycosis, as the micro-organisms tend to arrange themselves in different ways at different times. W. Silberschmidt (Deutsche med. Woch., Nov. 21, 1901).

At a certain stage there are in every colony three elements, viz.:—

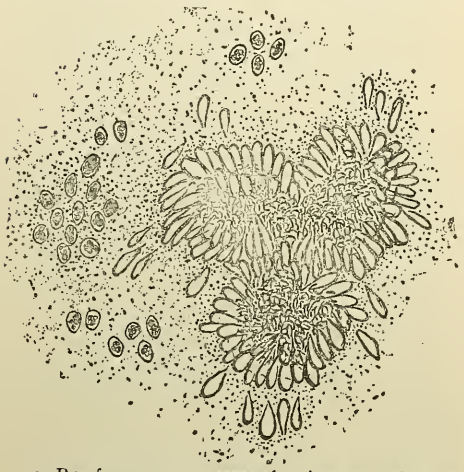
1. Club-shaped formations.

2. A centrally placed network of fungous filaments of varying shape and size.

3. Fine coccus-like bodies (spores), which originate from the fungous filaments, and grow into long rods and branching twigs.

Two types, the typical and atypical, should be recognized, according to Berestneff. Typical actinomycosis is the disease in which occur the characteristic mycelial masses, having club-shaped radiations. Atypical actinomycosis includes such diseases as Nocard's *farçin de bœuf,* and infections which clinically and anatomically resemble actinomycosis, and are caused by branching mycelial organisms which correspond quite closely to the cultural peculiarities of the streptothrix actinomyces, but fail to form the characteristic grains in the tissues and pus.

Case of streptothricosis, a disease of man or animal due to one of the various forms of streptothrix. The manifestations of the disease probably differ in accordance with the forms of causative organism. If organisms of thread form are present the surgeon can be reasonably sure of the diagnosis. If the threads are branched he can be certain of it. The ray fungus is seldom found in humans, and is not invariably found in bovine streptothricosis. The appearance of the disease varies with the stage in which it is seen. A description of the surface appearance



a, Ray-fungus or masses, showing central mycelium of actinomycosis. *b*, White blood-corpuscles, showing their relative size. (*Poncet and Bérard.*)

of an early stage would by no means fit a well-developed or an advanced case. The appearance is greatly changed by mixed infection with pyogenic bacteria. A severe secondary pyogenic infection may obliterate all appearances suggestive of streptothricosis, and in such a case it may be impossible to demonstrate the streptothrix. Certain persistent abscesses, particularly abscesses connected with the alimentary tract, are due to streptothrix infection and secondary infection with pyogenic bacteria. J. Chalmers Da Costa (Annals of Surg., July, 1911).

Staining.—The following stains have been used:—

Wedl's orseille (Weigert).

Eosin (Marchand).

Cochineal—red (Dunker and Magnussen).

Hematoxylin alum (Moosbrugger).

Gram's method—section staining (Partsch).

Safranin in aniline oil, followed by K. I. (Babès).

Solution of orcein in acetic acid (Israel).

Picrocarmin—fungus, yellow; other parts, red (Baranski).

The actinomyces in a section are best shown by Gram's method, first with methyl violet, then with Bismarck brown (Tillmann).

Cultivation.—It is quite difficult to cultivate in coagulated blood-serum (O. Israel), coagulated blood-serum and agar-agar (Boström), and coagulated egg-albumin and agar-agar (Wolff and J. Israel).

INOCULATION.—It has been successfully carried out by James Israel and Ponfick, from tissue and from pure cultures.

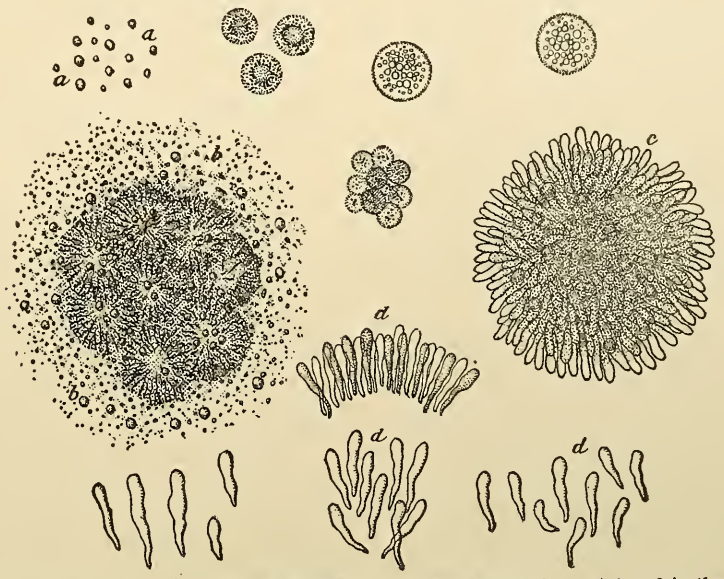
Opinions differ as to its power of producing pus, a secondary infection by the pus-germs being thought the true cause of the pus sometimes found with actinomycosis. Dissemination by the lymphatic system never occurs. Glandular enlargement indicates secondary infection.

1. Cutaneous Surface.—Around the primary lesion are small secondary lesions. Two forms are described: (*a*) The anthracoid, which pursues a rapid course, with fever, and sometimes septicemic in character. It is characterized by flat tumefaction, with multitudes of small openings with yellow granulations, from which thick pus exudes. (*b*) The ulcerofungous, which pursues a subacute course, with tendency to chronicity. In the face it tends to form

burrowing abscesses instead of recognizable tumors.

2. Bronchial Tubes and Lungs.—Some observers believe that the peribronchial lymphatic vessels and glands disseminate the fungus or its spores in the lungs; when the fungus reaches the lung-tissue proper, granulation tissue is formed, which, through secondary infection, suppurates. Amyloid degeneration of other organs may occur, or

Actinomycotic growths in the liver in man, according to Crookshank, have a characteristic naked-eye appearance, from their peculiar honeycombed structure. The cases between the fibrous trabeculæ are full of caseous matter, in which the more or less spheroidal masses of the fungus are imbedded. In museum specimens, which have been for some time preserved in spirit, the contents of the loculi may have fallen out,



Ray fungus (*c*, *c*, *c*), club-shaped bodies (*d*, *d*, *d*), and spores (*a*, *a*, *a*) found in the pus of actinomycosis. (*Poncet and Bérard.*)

metastasis of the disease, in case a pulmonary vein has been pierced. At times the pericardium or peritoneum becomes affected (Strümpell).

3. Alimentary Canal.—In the jaws the mass usually resembles a sarcoma, but, if incised before secondary infection and suppuration has occurred, the reddish surface will be seen to be intermingled with yellowish spots, which are collections of actinomyces.

In the intestines the fungus causes proliferation of the submucous tissue, and whitish patches. External fistulæ are commonly found.

and the honeycombed appearance is then much more marked than in recent specimens.

The writer having noted the frequency of the organisms in sputum, their failure to grow at other than body temperature, and the lack of convincing evidence that the disease was contagious, these facts suggested that the infection arose within the individual. The prevailing location of the diseases about the jaw or neck pointed to the mouth as the source of infection. In addition, the history of much trouble with the teeth, preceding the infection, was conspicuous in two of the author's cases of acti-

nomycosis. Following this line of thought, he made careful microscopic, cultural, and biological examinations of the contents of carious teeth removed in 16 examined cases. In all 11 cases by cover-slip preparations, Gram-staining filaments mixed with other bacteria were found. Serial sections studied in 5 cases were positive. The organisms were present in such numbers as to suggest that they play a fundamental part in dental caries. Lord (Boston Med. and Surg. Jour., July 21, 1910).

PROGNOSIS.—The prognosis is serious in proportion to the rapidity with which suppuration occurs. Actinomycosis of the upper jaw is more serious than actinomycosis of the lower jaw, as it has a greater tendency to invade the deep structures. Internal actinomycosis is almost always fatal, owing to its inaccessibility. External actinomycosis may cause death from pyemia, septicemia, and exhaustion. When so placed as to be easily removed and treated early the prognosis is favorable. A permanent recovery usually follows a complete removal of the primary focus, as metastasis is rare (Senn).

Actinomycosis has a pronounced tendency to spontaneous recovery except in internal organs (Schlange).

From an analysis of 60 cases the following conclusions are reached: When the disease involves the head and neck, except in a few cases when the base of the skull is invaded, the course is favorable, recovery taking place in from three to nine months. It is exceptional for the fistula to persist or to form anew after the lapse of a year. Pulmonary actinomycosis may terminate in recovery. The prognosis of actinomycosis is the more favorable, as the anterior abdominal walls are involved and the posterior escape. Death usually results from amyloid degeneration and wasting. If actinomycosis presents pyemic manifestations, a fatal termination is to be expected, as a number of vital organs are likely to be involved. Actinomycosis may pursue a chronic course, continuing thirteen years or longer, if functionally important organs be not involved, as when the process confines itself to the connective tissue about the spinal column.

> The prognosis, as shown by a study of all cases reported, depends largely upon the location of the disease, the pulmonary cases showing the highest mortality, the cervicofacial the lowest. W. G. Erving (Bull. Johns Hopkins Hosp., Nov., 1902).

> The prognosis is now much better than formerly, some cases recovering spontaneously. If surgical treatment is not possible the prognosis is grave, but not always hopeless. If the diseased tissue can be reached it should be incised, scraped, cauterized with nitrate of silver stick, the cavity packed with iodoform gauze, and iodide of potassium given internally in large doses. The X-ray should subsequently be used. Bevan (Annals of Surg., May, 1905).

TREATMENT.—1. General.—Potassium iodide was found useful in animals by Thomassen and Nocard. In man it should be thoroughly tried before surgical intervention is resorted to, especially when the disease is so extensive as to prevent complete removal by surgery. The results obtained from iodide of potassium have been remarkable in some cases and negative in others. This divergence of views, according to Pernet, depends on the variation in the virulence of the disease, in its evolution in different individuals, in the difference existing in the receptivity of the tissues, and on the influence of secondary infective processes. In recent and purely actinomycotic lesions the results may be

excellent; in old-standing cases, and where the ray fungus is associated with streptococci, staphylococci, and the bacterium coli commune, the drug treatment is less successful.

According to Bérard, in two-thirds of the cases of chronic actinomycosis of the face and neck the results of iodide treatment are *nil*. In three-fourths of the recent cases recovery has been obtained by it, combined with surgical treatment, and in one-fourth by iodide treatment alone. Potassium iodide cannot be regarded as specific in actinomycosis in man. If, at the end of some weeks, improvement is slight only, operative interference should be carried out at once.

The drugs which are the most successful in pulmonary actinomycosis, in the opinion of Sabrazès and Cabannes, are **potassium iodide** and **eucalyptus**. If there is any involvement of chest wall, surgical treatment should be undertaken.

Four cases, in one of which the tumor was situated below the angle of the scapula. All the patients were given **iodide of potassium**, and the wounds were treated with **peroxide**, tincture of **iodine** in full strength or solution, and packed in **iodoform gauze** until all evidence of presence of the fungus had disappeared. J. C. Munro (Boston Med. and Surg. Jour., Sept. 13, 1900).

The injection of a 5 per cent. solution of **permanganate of potassium** into the cysts has been of advantage.

Case of actinomycosis of the face which was cured by **hot compresses** (temperature, 63° C., or 145° F.) and **carbolic acid** injections. The first dose of the latter was 12 c.c. of a 3 per cent. solution. The compresses were continuously applied day and night, being changed every ten minutes. A. Strubell (Münch. med. Woch., May 8, 1900).

While **potassium iodide** in connection with the **X-ray** exerts a curative effect in superficial actinomycosis, this treatment is, to a great extent, without avail in pulmonary and abdominal involvement. Hence **copper sulphate**, which is used to destroy the fungi of grain and other vegetable parasites, tried in doses of ¼ to 1 grain three times a day. Good results obtained both in blastomycosis of the skin, where the copper is given internally and used as a wash of 1 per cent. strength for the lesions, and in actinomycosis, where it is also given by mouth, and a 1 per cent. solution is employed in irrigation of sinuses. A mixed treatment of **copper** and **iodine salts** may prove most effective in certain cases. A. D. Bevan (Jour. Amer. Med. Assoc., May 20, 1905).

Great difference of opinion exists as to the value of **iodide of potassium** in the treatment of actinomycosis. The important point is to use the drug at a time when there is a chance of eradicating the disease. Cases in the advanced stages of the disease may be benefited by its use, but the possibility of a cure is an extremely remote one. Whether the simple treatment of opening the abscess and draining it would be sufficient for a cure, it is impossible to say, but in this case the fact remains that the patient did not begin to improve until she was thoroughly under the influence of the drug. The action of the iodide in this disease is unknown; possibly by promoting absorption of inflammatory products as they are formed it may check the spread of the disease. So far as known, it can have no specific action on the organism of actinomycosis. Iodides are largely used in the treatment of this disease in veterinary practice, and many cures have resulted. Knox (Lancet, Nov. 3, 1906).

Actinomycosis of the appendix is usually chronic and may last for years. If possible, the cecum and neighboring bowel should be sacrificed for a thorough removal of the

disease. Usually all that can be done is to **open abscesses** as they point, and to give internal remedies, as **potassium iodide**, etc. Short (Lancet, Sept. 14, 1907).

Six cases of actinomycosis apparently cured by injections of **sodium cacodylate**. The infection originated always from the cavity of the mouth, with localization of the abscesses and infiltration on the tongue; the neck, with perilaryngeal spreading; in the regio temporalis, with spreading to the base of the skull, and of the lower jaw, with spreading to the submaxillary glands. On the first day a 10 per cent. watery solution (¼ of a Pravaz syringeful) was injected intramuscularly in the nates, increasing each day ¼ syringeful until a full syringeful is given during one week, and then decreasing the quantity to the ¼ syringeful, and then commencing over. The local measures are confined to **puncture** or little **incisions** for abscesses. More extensive operations are avoided. Foederl (Zentralbl. f. Chir., Bd. xxxv, p. 45, 1908).

Experience in 56 cases in which treatment was by **iodide** alone, with 34 cures; 94 with operation alone, with 75 cures; 109 with **excision plus iodide**, with 60 cures, and 30 in which treatment was by other measures, with 25 cures. All but 46 of the cured patients have been re-examined recently. The writer calls attention to the fact that the deaths during the years since were, in many cases, reported as having been due to tuberculosis, while there is a possibility that the supposed tuberculosis may have been merely a metastasis in the lung from the old actinomycotic infection in some of these cases. His conclusions from a review of nearly 300 cases are that actinomycosis, when circumscribed, should be resected like any other tumor. If this is not possible, or if the affection is diffuse, he advocates administration of **sodium iodide** internally, with partial **resection**. His experience in one case encourages further trials of tuberculin in actinomycosis, as the cure in this case can be ascribed, he thinks, only to the course of tuberculin treatment. The iodide does not require such large dosage as some advocate; his preference is for 1 Gm. the first day, 2 Gm. the second, 3 Gm. the third (from 15 to 45 grs.), repeating the same succession after suspension for three days. Sometimes he gave from 2 to 5 Gm. a day in powders, supplemented by local applications of a 10 per cent. solution of **sodium iodide**. Maier (Beiträge z. klin. Chir., June, 1909).

2. **Surgical.**—Local measures which do not completely remove the infected tissues do harm, as they frequently give rise to secondary infection, rapid extension, and death.

Cauterization with solid silver nitrate in actinomycosis of skin and soft parts in which suppuration and fistulous tracts have occurred possesses a specific action on the actinomycosis (Köttnitz).

3. **Electrotechnical.**—Two platinum needles, attached to the two poles of a constant-current battery, are to be inserted into the tumor. Through the two needles a current of 50 milliampères is to be passed, while every minute some drops of a 10 per cent. iodide of potassium solution are to be injected into the mass. The solution is decomposed into nascent iodine and potassium. This is repeated every eight days, each session lasting twenty minutes, under an anesthetic (Gautier).

Before suppuration all diseased tissues, glands, etc., should be removed and the parts, when possible, cauterized with the thermocautery.

After suppuration the parts should be treated as if they were tuberculous, curetting and packing with **iodoform gauze**.

Ernest Laplace,
Philadelphia.

ACTINOTHERAPY. See Light.

ACTIVE HYPEREMIA. See Hyperemia, Bier's Treatment by.

ACTOL, or silver lactate, occurs in the form of a white powder, odorless and almost tasteless, which is soluble in 15 parts of water. Its color is changed when exposed to the light. Applied to the tissues, it causes coagulation of the proteids, in common with the nitrate of silver.

THERAPEUTICS.—Actol has marked **antiseptic** and **disinfectant** properties, according to the strength of solution used. In solutions of 1 in 500 to 200 it is used as an antiseptic for wounds. For infected wounds it may be employed as a disinfectant in stronger or even saturated solutions. But little discomfort is caused when the powdered silver lactate is applied to open surfaces. It is claimed to have a deep-seated effect by penetration to the subjacent tissues, though known to be decomposed into other compounds when in contact with the superficial cells. Actol has also been used internally as an antiseptic. It has been found effective in diminishing intestinal putrefaction, at the same time causing a tendency to constipation. Some have even employed it internally and hypodermically for a general antiseptic action throughout the organism. Sixteen grains (1 Gm.) have been injected subcutaneously without serious results. S.

ACUPUNCTURE.— This procedure is principally used for the relief of tension in edematous or congested tissues. It is especially useful in edema of the scrotum, labia, and extremities when the tissues are sufficiently distended to threaten sloughing. Acupuncture is also employed for the relief of pain in neuritis and muscular rheumatism, especially in sciatica and lumbago; the benefit afforded, when such is obtained, is due mainly to reflex contraction of the blood-vessels of the area, thus reducing the congestion of the nervi nervorum and the sensory terminals to which the pain is due. In edema, the benefit is the direct result of the abstraction of considerable blood-serum imprisoned in the tissues.

TECHNIQUE.— The instruments employed are a very small narrow-bladed bistoury and surgeons' needles. The part should be carefully sterilized by first washing it with soap and water and then bathing it with alcohol or a 1:2000 solution of mercury. The operator's hands and instruments should likewise be carefully sterilized. These precautions are very important in view of the fact that edematous tissues are readily infected. If the patient is very sensitive to pain, the part may be anesthetized with ethyl chloride.

For **edematous tissues** the small bistoury is the better instrument, one or two stabs, or, in large areas, many such, being practised, avoiding blood-vessels. A compress dipped in a warm 5 per cent. solution of boric acid is then applied to encourage escape of the serum. These must be frequently changed and the tissues kept very clean, as otherwise fetor soon appears.

For **muscular rheumatism,** especially **lumbago,** a number of round needles are thrust into the painful area from 1 to 2 inches, according to the fat overlying the part, and left *in situ* from five to ten minutes. The pain often ceases at once. Great care should be taken, on withdrawing the needles, not to break them, lest fragments remain in the tissues. In **neuritis, sciatica,** etc., the needles, several of them are thrust into the nerve sheath at intervals (not a difficult procedure in large nerves) and left *in situ* about five minutes. A fine hypodermic needle may be used, among the ordinary needles, with advantage, in the same way, and increase the efficiency of the treatment by being used to inject a little sterile water, which acts as an analgesic, or, if the pain be very severe, morphine. This treatment is efficacious in most instances where other measures have failed. S.

ACUTE RHINITIS, OR ACUTE CORYZA.—DEFINITION.—An acute inflammatory condition of the nasal mucous membrane, in which repeated attacks predispose to the extension of the inflammation to the neighboring cavities, as the pharynx; the larynx; the lower air passages; and to a lesser degree, to the accessory sinuses of the nose.

SYMPTOMATOLOGY.—The earliest manifestation of an acute rhinitis

is a sensation of dryness or irritation in the nose, which later becomes of an itching, tickling, or stinging character. Very often the attack is ushered in by a preliminary chill or "a creepy feeling." Sneezing is an early symptom, and is soon followed by a sensation of fullness in the nose, with subsequent obstruction to nasal breathing, and a dull throbbing headache over the site of the accessory cavities. A general feeling of illness, with aching in the limbs and back, frequently prevails. The sense of smell and taste are interfered with. Hearing is often markedly impaired, owing to the involvement of the mucous membrane at the orifice of the Eustachian tube, or the extension of the inflammation through the tube into the middle ear. The voice is also altered and assumes a nasal intonation. There is a noticeable loss of resonance which characterizes the normal voice, and the sounds of *m* and *n* cannot be readily produced. The skin is dry and at times becomes hot from the presence of fever.

Thirst and anorexia are also associated symptoms. The urine is scant and high colored. The existing constipation is usually responsible for the presence of the furred tongue. The eyelids are more or less swollen from the existing congestion, and a profuse lachrymation is not infrequently present from the extension of the inflammation through the nasolachrymal duct. The membrane of the nose is red, swollen, dry, and glazed, and is unduly sensitive. The nasal passages are practically occluded by the swelling of the membrane and the erectile tissue of the turbinates to the capacity of the fossæ, thereby greatly interfering with the normal physiological functions of the nose, as well as with that of deglutition. Owing to this existing obstruction, nursing infants at times manifest considerable difficulty in obtaining sufficient nourishment.

The nasal discharge at first is scant, or it may be entirely absent, but it soon becomes copious, is clear, and, owing to the presence of an excessive amount of salines in its composition, it becomes very irritating to the skin of the upper lip and the nasal alæ; in fact, the irritation not infrequently becomes so marked as to cause excoriation, or even cracking, of the bordering cutaneous surfaces. This condition, no doubt, is often very much aggravated by the frequent use of the handkerchief.

As the disease progresses, the discharge becomes opaque, mucopurulent in character, thick and tenacious, and of a greenish-yellow color. A microscopic examination of the discharge shows a marked increase in the corpuscular elements.

No sharp line of demarcation exists between the second and the terminal stages of this disease. In three or four days the discharge gradually becomes thicker and scantier; the swelling of the membrane subsides; the constitutional manifestations gradually lessen and finally disappear; the special senses assume their normal activity, and in the course of a week or ten days all traces of the disease disappear.

A significant feature of acute rhinitis is the possibility of the antrum of Highmore, the frontal sinus, the ethmoid or the sphenoid cells, the Eustachian tube, or the middle ear becoming the seat of disease as the result of the extension of the inflammatory process. The nasopharynx and the pharynx invariably become involved, partly through the extension of the inflammation by continuity, and partly from the interference with the normal function of the nose.

DIAGNOSIS.—The recognition of this condition, as a rule, is seldom fraught with many difficulties, and the diagnosis in most cases is usually made with considerable ease. It is important, however, to guard against the possibility of a mistake by making careful inquiry into the history of the attack, and also by making a cautious examination of the nasal cavities in order to distinguish between a simple acute catarrh and a rhinitis as the result of measles, influenza, nasal diphtheria, hereditary syphilis, a foreign body, a tumor, and iodism. Cases of measles and influenza will invariably show a higher temperature and greater constitutional disturbances, and in the former case the appearance of the rash will eliminate all doubt of the cause of the existing nasal condition. Nasal diphtheria can be recognized by the existence of the characteristic grayish membrane in the anterior nares and in the throat, associated with the usual constitutional symptoms. In the absence of the membrane, strong evidence of the condition continues to exist in the blood-tinged discharge, but a positive diagnosis can be obtained only by culture. The "snuffles" of hereditary syphilis is usually found in very young children, with concomitant symptoms of this infection, *i.e.*, malnutrition, glandular enlargement, and in older children the characteristic Hutchinson's teeth. A foreign body or a tumor can be detected on examination, and in cases of iodism a careful history will elicit the fact that a considerable quantity of the drug has been taken.

Cases of acute rhinitis are occasionally encountered in which the causative agent is some chemical irritant. The diagnosis should not be difficult, as constitutional symptoms are rarely resent; the duration of the attack is seldom, if ever, as long as the ordinary cases; and with the withdrawal of the cause the condition invariably subsides.

The patient seldom seeks treatment for acute rhinitis much before the end of the first or the beginning of the second stage of the disease, and then gives a history of exposure, quickly followed by the nasal discomfort and the rapid development of the disease. This history, in conjunction with the more or less characteristic appearance of the conditions within the nasal chambers, will usually be sufficient evidence for a positive diagnosis.

ETIOLOGY.—Predisposing Causes.—If careful observation were made in each case of acute rhinitis, it would, no doubt, frequently be seen that the attack occurs when the resisting powers of the body are below par. Under normal conditions a certain equilibrium is maintained for the production and the elimination of the waste products of the body; but, when, for some reason, the normal function of this apparatus is interfered with and there occurs a faulty elimination of the waste products or an overproduction of the same, body resistance is lowered and susceptibility to disease becomes more marked. This condition is undoubtedly often encouraged by indiscreet action of the patient in regard to diet, causing digestive disturbances, torpid liver, and constipation, in which the consumption of food is out of proportion to the combustion, thus causing an autotoxemia, in which there is sometimes a marked evidence of uric acid. It is at this time that a coryza may be considered the nasal signal of systemic poisoning, for the blood will be found tainted with the products of faulty oxidation. Strong evidence of this condition will also be

found in the examination of the urine, in which uric acid or mixed urates will be present.

With such lowered resistance, one becomes easily affected by conditions such as prolonged confinement in an ill-ventilated room, extreme physical exhaustion following overwork, or a severe mental strain. A lowered nervous tone; interference with the normal activity of the sudoriferous glands, and the absence of a natural covering for the head, as in baldness, are oftimes important predisposing factors.

> Acute coryza is the result of a triple pathogenetic alliance—a chronic rhinitis, a chronic intestinal toxemia, and an exposure to an accidental stress of some kind, not necessarily thermometric or hydrometric, for just as effective as these are others of an emotional, dietetic, dynamic, or microbic nature. Although in all cases the general principles of treatment will be the same, considerable discrimination in the matter of detail must be exercised in the individual case, because of the varying nature of the exciting cause. Grayson (Therap. Gaz., May, 1909).

It is not uncommon to find in some patients showing a disposition to frequent colds some underlying pathological condition within the nose, such as deviation of the septum, a stenosis, or a hypertrophic rhinitis, thus causing the current of air to be misdirected in such a way as to act as an irritant upon a more or less sensitive membrane, which is usually below par as the result of recurrent attacks.

When frequent and persistent attacks occur in childhood, a careful examination of the nasopharynx will sometimes show the causal agent to be the existence of adenoids. Acute rhinitis is not infrequently found in infants under three months and those who are suffering from malnutrition, as in rachitis. It is also thought by a noted pediatrist to be a complication of dentition. In susceptible children, the cause is often very trivial. A curious fact exists in that this affection is seldom found in old people.

An hereditary tendency seems quite apparent in some cases, notably in children. In the majority of cases, however, the direct cause can be traced to an improper mode of living. The child gets very little fresh air; is confined in a room which is improperly ventilated, usually overheated; the windows of the bedroom are kept carefully closed at night for fear the child may catch cold; the clothing is very often in excess of what is really needed, thus making it impossible for the individual to indulge in any active play without producing a profuse perspiration. Under these conditions the mucous membrane, especially of the nose and throat, soon becomes very sensitive and the child is a frequent sufferer of colds.

Evidence sometimes point to such chronic conditions as asthma, hay fever, rheumatism, tuberculosis, and syphilis as being factors in the production of acute rhinitis. Attacks in some persons can be attributed only to their idiosyncrasy. Excessive sexual indulgence often shows a predisposition to provoke an attack, as do gastric and intestinal diseases, and a neurotic tendency. Thermic and climatic conditions are sometimes to be considered.

Exciting Causes.—Although certain depraved conditions of the body may be said to predispose to attacks of acute rhinitis, usually there are certain causes to which the attack may be definitely attributed. Exposure to cold and wet when the body is overheated; exposure to sudden or extreme changes in the atmosphere; the wetting of the feet

when the system is debilitated from other diseases; or the chilling of the body from any cause, especially as the result of sitting in such a position as to allow a draft of air to strike the back of the neck or head. This seems to support the theory advanced by some that the impression of cold on certain parts of the body produces an inhibitory effect upon the vasomotor nerves controlling the blood supply of the nasal mucous membrane.

The inhalation of certain irritating chemical fumes, such as those of iodine, chlorine, bromine and hydrochloric acid may result in a coryza. Sometimes the mere inhalation of irritating dust may produce an attack. Foreign bodies in the nose; or certain drugs, as ipecac and the iodides, may produce the same effect. Wagner is of the opinion that the inflammation is not infrequently the result of migration of bacteria from diseased tonsils. The examination of the nasal secretion often shows the presence of a variety of micro-organisms, chief among which are the *Micrococcus catarrhalis,* the *Bacillus septus,* the *Bacillus Friedländer,* and the *Bacillus segmentosus* of Cautley.

> There are several kinds of organisms capable of causing a cold. This term does not, therefore, answer to one specific malady, but connotes several distinct maladies which it is convenient to group together under a generic name. Among the more common "cold" organisms are the following: Friedländer's bacillus; the *Bacillus septicus;* the bacillus of influenza; the *Micrococcus catarrhalis.* These organisms give rise in the susceptible to specific febrile disorders; but, unlike the exanthemata, these disorders do not confer immunity for more than a very limited period, sometimes for not more than a few weeks. Campbell (Practitioner, Oct., 1909).

> The evidence seems indicative that the diphtheroids, particularly *Bacillus segmentosus* of Cautley, are concerned in the production of so-called common cold in its typical manifestations in the nose, and there is much evidence that it occurs in epidemic form. The *Micrococcus catarrhalis* is much more general in its manifestation, and is, probably, also epidemic and productive of a rather more severe inflammation, though mild epidemics occur. It seems likely that the symbiosis of these two organisms increase the virulence. The pneumobacillus of Friedländer is much more concerned in chronic conditions and is probably identical with the ozena bacillus. The pneumococcus of Fränkel flourishes in any part of the upper respiratory tract and, when virulent, has been found in pure culture. Clinically, the segmentosus infection is most likely to be in the nose, seldom in the trachea, but may cause otitis media; *Micrococcus catarrhalis* is most apt of all to invade the larynx and trachea, but may occur in the ear or nose and with variable virulence. The pneumobacillus is mostly confined to the nose and sinuses. Influenza is conspicuous by its absence. Pyogenic cocci are non-pathogenic locally, except as secondary invaders, and the probability is that only a limited number of strains are concerned in causation of acute infections of the mucosa, and these are not genuine coryza. The bacterial flora of the nose in America probably do not differ materially from those of other countries, but must of necessity be governed largely by environment, occupation, social position, and epidemics as to the ratios of finding. W. Walter (Jour. Amer. Med. Assoc., Sept. 24, 1910).

Whenever the disease is at all prevalent, suspicion arises as to the possibility of it being contagious or produced by some infectious material in the air. It not infrequently ushers in an attack of bronchitis, laryngitis, or one of the acute infections, such as influenza, measles, typhoid fever, smallpox, or whooping-cough.

PATHOLOGY.—An acute rhinitis is characterized by the same pathological changes which take place in inflammation of the mucous membrane elsewhere in the body, and may be considered in three stages.

Stage of Engorgement.—During this stage the mucous membrane is swollen and rather dark in color. The normal secretion at first is decreased, or even entirely arrested, and there occurs a proliferation of the epithelium. If the microscope could be used at this time, the blood-vessels would be seen to be markedly dilated and there would be more or less stasis of the blood-stream, permitting the adhesions of leucocytes to the blood-vessel walls. Their final penetration into the surrounding tissue is the beginning of the next stage.

Stage of Exudation.—With the migration of the leucocytes into the interstitial tissue, there is also a transudation of altered blood-serum and a forcing out of erythrocytes. The discharge that follows is usually profuse; at first it is a mixture of mucus and serum, but this soon becomes of a mucopurulent type and finally purulent.

Stage of Resolution.—This is characterized by the restoration of the normal function of the mucous glands, the secretion from which causes the discharge to become thicker and more opaque. The exudate within the mucosa is gradually absorbed, the lost epithelium in time is replaced by new cells, and the membrane is slowly reduced to its normal size.

PROGNOSIS.—This depends upon the severity of the attack and the extent to which the tissues are involved. The simple cases usually recover in the course of a few days to a week without any detrimental results. In some few cases, however, certain changes may take place in the tissues and increase their tendency to recurrent attacks. The prognosis becomes less favorable for an early recovery if the inflammation should extend into any one of the accessory cavities of the nose and cause a suppurative process, or if there should occur an involvement of the middle ear by extension through the Eustachian tube.

TREATMENT.—The treatment of acute rhinitis may be prophylactic, abortive, or curative, depending upon the cause of the attack. Persons who show a predisposition to recurrent attacks of coryza should guard the body against such conditions as favor their onset. The protective agencies of the body should be strengthened by regular and systematic exercise, especially in the open air, and should be of the nature of horseback riding, golf, tennis, or something as vigorous. Grayson recommends, instead of medicine, good **vigorous exercise** several times a day, claiming that "the quickened capillary circulation and vigorous action of the sweat glands that accompany hard exercise are incomparably more beneficial than the merely passive leakage that follows the use of diaphoretic drugs. If in addition to this an **abundance of water** is drunk and the supply of **food** is greatly **reduced**—almost stopped in fact—we may look for an amelioration of all the coryza symptoms in a much shorter time than if our main reliance is vested in quinine, belladonna, and opium combinations, that have had too long a vogue."

Proper **discretion in diet** should be practised, particularly by those who are victims of uric acid diathesis. **Cold bathing**, gradual at first, is an efficient stimulant to the relaxed vascular system. Proper selection of underwear

and clothing, especially for outdoor service, should be made.

If the patient is seen in the early stages, in the first few hours, the attack may be abbreviated, or the duration, at least lessened, if the proper treatment is immediately instituted. The patient should be given a **mustard foot-bath,** 4 grains of **quinine,** 10 grains of Dover's **powder,** a **hot lemonade,** and then put to bed with a liberal covering of bedclothes to encourage free perspiration. This should be followed by active **catharsis.** The above treatment will usually necessitate the keeping of the patient in the house at least the following day.

Recent investigations lead to the belief that the isolation of the predominating organism from the nasal secretion and the injection into the patient of a **vaccine** product from the same will frequently abort an attack, and even establish a certain degree of immunity for a short period of time. The earlier the injection, the more decided will be the result.

> By means of **vaccine** therapy, not only are we able to cut short an acute cold, but also to confer considerable immunity against future attacks. By this method we can, further, often successfully treat colds which have become chronic, *e.g.,* chronic rhinitis, laryngitis, bronchitis, etc.
>
> In but few cases of common cold can a stock vaccine be employed with much hope of success; except in the case of the *Bacillus septus* we are not likely to do good by any vaccine other than that prepared from the patient's own person. Having secured the specimen it is forwarded to an expert, and the vaccine can be prepared ready for use within forty-eight hours of its receipt. The best time for the injection is the evening, and the best spot the flank slightly above and internal to the anterior superior spine. If the reaction is pronounced it may be necessary to keep the patient in bed for twenty-four hours. Campbell (Practitioner, Oct., 1909).

Early convalescence and the return of the normal vigor will be augmented by the administration of **tonics,** strychnine and quinine being two of the favorite remedies. After two or three days this treatment is not sufficiently efficacious and curative measures will have to be resorted to.

The usual run of cases can be cured without confining the patient to the house, unless the weather is severe. In children, however, an attack which may be considered mild in an adult may be severe enough to confine the young patient to bed. On the first visit of a case of acute rhinitis, especially if early in the disease, the nasal discharge will be found thin and acid, and the mucous membrane markedly swollen. Reduction in the size of the turbinal bodies can be obtained by the application of a 1 per cent. solution of **cocaine** and a 1:10,000 solution of the **suprarenal extract.**

A solution of 2 per cent. **cocaine** and 2½ per cent. **antipyrin** often acts to greater advantage in these cases, as the latter remedy prevents a violent reaction and frequently prolongs the contraction.

In patients who are sufferers from gout, the **cocaine** will invariably fail to produce the desired reduction of the mucous membrane, but relief may be obtained by the free administration of **colchicum.**

Cocaine should be used with the greatest care in infants, as they are particularly susceptible to its detrimental effects. Weak solutions are permissible, however, when the symptoms are severe and the infant is pre-

vented from nursing. Powders containing **cocaine** are often prescribed for adults; but it has caused cocainomania in so many cases that it should only be applied by the physician himself with an insufflator to cause contraction of the mucosa and the effect kept by means of a powder containing no cocaine which the patient can use as snuff.

For use by the physician the following is efficient:—

℞ *Cocaine hydrochloride,*
Camphor .....āā gr. j (0.065 Gm.).
Pulverized sugar.... ʒij (8 Gm.).
Morphine hydrochloride ..... gr. j (0.065 Gm.).
Pulverized acacia,
Bismuth subnitrate.āā ʒj (4 Gm.).
Pulverized mallow... ʒiss (6 Gm.).

Enough to cover a dime to be insufflated in each nostril.

Ointments may also be used conveniently by the physician, by means of a flat probe. Lemoine recommends the following formula:—

℞ *Cocaine hydrochloride,*
Salol .....āā gr. ⅓ (0.021 Gm.).
Menthol ..... gr. ss (0.032 Gm.).
Boric acid ..... ʒss (2 Gm.).
Petrolatum ..... ʒj (30 Gm.).

A piece the size of a large pea is applied with the probe to the swollen mucosa in each nostril.

Insufflations may be made with:—

℞ *Calomel,*
Morphine hydrochloride .....āā gr. ⅙ (0.01 Gm.).
Bismuth subnitrate .. ʒiiss (10 Gm.).

To sustain the effect Rudaux, Grosse and le Lorier recommend the instillation into each nostril, night and morning, of several drops of the following solution:—

℞ *Eucalyptol* ..... gr. ⅘ (0.05 Gm.).
Sterilized liquid vaselin ..... ℥j (30 c.c.).

On the other hand, Weitlauer, of Innsbruck, commends the internal use of sodium salicylate, combined with Dover's powder, which, it is said, will afford relief one hour after beginning treatment:—

℞ *Sodium salicylate*..... ʒj (30 Gm.).
Dover's powder ..... gr. xlv (3 Gm.).
Spirit of peppermint... ♏j (0.06 c.c.).

To be divided into 20 powders, 1 of which is to be taken in a little water every three or four hours.

Aromatic spirit of ammonia and **sweet spirit of niter** are recommended as excellent agents to "abort" a cold by Beverley Robinson.

> One or two doses of 1 Gm. (15 grains) each of **acetylsalicylic acid,** taken at the first indication of an oncoming cold in the head, will arrest it. The drug is especially effectual when the first tickling in the throat is felt toward evening, and the drug is taken then and again in the morning. This permits him to go about his surgical tasks after breakfast without any further symptoms of coryza. If acute rhinitis has developed or the coryza relapses, two or three further doses always cured it completely. The drug probably does not act on the bacteria, but it seems to enhance the resisting powers of the tissues. Sick (Münch. med. Woch., July 16, 1912).

At home the patient should be instructed to use one of the well-known cleansing sprays, such as **Dobell's solution, glycothymoline,** or a solution made from **Seiler's tablets.**

A very useful and economical solution is prepared by dissolving a teaspoonful of salt in a pint of water—practically a **normal salt solution**—and using it freely in the nose.

In using any cleansing solution, great care should be exercised in blowing the nose directly afterward, for when it is done too harshly some of the solution mixed with the nasal secretion may be

blown into the middle ear through the Eustachian tube and set up an inflammation with the formation of an abscess.

Following the cleansing, the inflamed mucous membrane may be protected by an oily solution composed of:—

℞ *Menthol,*
Camphor .....āā gr. v (0.3 Gm.).
Liq. albolene..... f℥ij (60 c.c.).

This is to be sprayed in the nose, or several drops may be placed in each nostril, and snuffed up, several times a day. If it is found impossible to drop the solution in the nose of a child, the application may have to be made by a brush.

Another useful combination is:—

℞ *Menthol* ..... gr. viiss (0.5 Gm.).
Phenylsalicylate .... ℥ss (2.0 Gm).
Boric acid ..... ℥ij (8.0 Gm.).
M. fiat pulvis.

Since the swelling of the mucous membranes renders the snuffing up of the powder difficult, the patient will find it advantageous to use a piece of rubber tubing about 20 cm. long; the powder is placed in it at one end, and air blown through from the other end by the mouth.

An excellent agent to keep the swelling of the mucosa down is the **adrenalin ointment** 1 : 1000, a piece as large as a pea being applied in each nostril.

During the early stage of the disease, when the nasal discharge is watery, one of the coryza tablets on the market can be used to good advantage to dry up the excessive secretion. This is particularly advantageous to those who are compelled to appear in public. A very satisfactory combination is the one devised and recommended by Dr. S. MacCuen Smith, which is made up as follows:—

℞ *Atropine sulphate* ..... gr. 1/600 (0.0001 Gm.).
Strychnine sulphate,
*Arsenous acid.*āā gr. 1/240 (0.00027 Gm.).
Morphine sulphate ..... gr. 1/100 (0.0006 Gm.).
Quinine sulphate. gr. 1/10 (0.006 Gm.).
Powd. camphor. gr. ¼ (0.016 Gm.).

By the time six of these are taken, at half-hour intervals, a dryness in the throat will be noticed. Only half of one should be given to a child of five years. Notwithstanding their known value among the laity, the indiscriminate use of these tablets should not be encouraged, for their administration at a time when the nasal discharge has become inspissated renders the patient much more uncomfortable and the discharge more difficult of expulsion.

In the third stage, when the membrane is relaxed and the epithelium is being shed more rapidly than it should, a spray composed of 20 to 60 minims of the distilled **extract of hamamelis** to the ounce of water may be used to good advantage.

It seems almost needless to state that the **diet** in all cases of acute rhinitis should be restricted at the beginning of the attack, but as convalescence takes place it can gradually be increased and finally restored to its normal status.

In those cases, and especially is this true in children, where there is a tendency to excoriation of the upper lip and the nostril, these exposed cutaneous surfaces should be protected from the irritating effect of the discharge by the application of **vaselin** or some simple ointment.

A mixture of **menthol** and **chloroform,** equal parts, is very efficacious. A few drops of the mixture are placed upon a handkerchief and inhaled through the nostril. It causes the obstruction in the nose to immediately disappear. A few drops may also be

placed in a cupful of hot water and the vapor inhaled. (Les Nouveaux Remèdes, March 24, 1910).

Sodium salicylate causes a cold to abort if taken within twenty-four to thirty-six hours. Single dose of 7½ grams (0.5 dram) often suffices. Taken later, it relieves symptoms and shortens attack. It is also valuable in the chronic coryza of gouty subjects. Should be taken after eating and preferably in small doses, dissolved in half a glassful of water. Courtade (Revue de thérap., Jan. 1. 1910).

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ADDISON'S DISEASE.—In 1855, Addison pointed out in a historic monograph ("On the Constitutional and Local Effects of Disease of the Suprarenal Capsules") the relations between a disease known as "bronzed skin" or "bronzed cachexia" and lesions of the adrenal bodies. The interest excited by this work at once called forth numerous observations on the subject, and, while a certain number of the papers lent support to the idea of close relationship between the lesion of the adrenals and the syndrome which Addison described, in others a contrary opinion was expressed. In the year succeeding the publication of his first monograph, Addison brought out a paper in which he described a lesion of the semilunar ganglia unaccompanied by changes in the adrenals.

We can thus state that it was Addison himself who originated the two theories which are still brought into requisition to explain the manifestations of the bronzed disease: the theory of adrenal insufficiency and the nervous theory. Before discussing these hypotheses, a study of the disease itself from the clinical aspect must first be made.

SYMPTOMS. — When Trousseau proposed that the term "Addison's disease" be applied to the affection described by the Scotch physician under the name "bronzed skin," he specifically designated "a singular cachexia especially characterized by the bronzed hue assumed by the integument." We therefore feel justified in including under the term Addison's disease only those affections which are of the "bronzed disease" types, and not the aggregate of all the conditions resulting from functional disturbances of the adrenals, *i.e.*, "without melanodermia, no Addison's disease." The disease, even thus limited, still presents a number of clinical forms showing rather well-marked special characteristics.

Asthenia.—The patient is generally unable to state the exact period of onset of the affection. In typical cases the pathological state is almost always one of adrenal tuberculosis which has invaded these organs secondarily, the patient is already in the wasting stage of tuberculosis, and it is difficult to recognize the new symptoms. Where there is primary adrenal tuberculosis, however, the symptomatology is more characteristic. Asthenia dominates the whole picture. The least physical effort is followed by extreme lassitude. At first the patient is still capable of energetic and rapid muscular activity, but he is not equal to sustained work; fatigue at once appears; later, as the process advances, lassitude becomes constant and the patient thinks of but one thing—avoiding the slightest exertion and remaining in bed in the dorsal decubitus. The mere ingestion of food requires an effort beyond the patient's strength, and the administration of solid food becomes difficult.

The earliest writers had been struck

by the asthenia of Addison's disease, and Jaccoud gave an excellent description of it. But the exact conditions under which this fatigue occurs were learned through the labors of Langlois, Charrin, and Abelous, who explained it on the basis of a new conception of its pathogenesis. The study of muscular fatigue with the ergograph of Mosso permits of differentiating the resistance in an ordinary case of tuberculosis from that in one of Addisonian phthisis. The simple tuberculous subject will continue lifting the weight of the ergograph for two minutes, performing total work equal to 1150 grammeters; the Addisonian subject, after having lifted the weight just as energetically during the earlier contractions, becomes fatigued very soon and stops exhausted before the second minute, having performed work equal to only 750 grammeters. If the weight to be lifted is placed at 2 kg., fatigue already appears at the fifth contraction and the sum of work done is practically *nil.*

Melanodermia, or *bronzing,* from which symptom the disease received its earliest appellation, often does not develop until after the asthenia. It appears most frequently in the form of small, brownish macules scattered over the entire skin-surface, though most marked at certain points of election. The scrotum and labia majora, which are normally pigmented, very frequently present a characteristic color. The mucous membranes are very often affected before the skin. The internal surfaces of the cheeks, the labial commissures, as well as the genital mucous membranes, should always be examined in asthenic subjects.

The melanodermia may remain localized, and this is, indeed, more usually the case, but it may also become generalized through confluence of the primary patches and involve the whole of the integument, making the patient's skin appear truly like that of a mulatto, though never like that of a full-blooded negro. Brault points out that the palms and soles are not involved, but these areas are imperfectly or not at all pigmented in negroes, and even in the anthropoid apes the soles of the feet remains of a pink color.

> Case of Addison's disease in a woman, aged 37, who complained of cough with expectoration and general weakness. The first sign was a very striking pigmentation of the skin. The color was yellowish brown, and affected chiefly the forehead, neck, hypochondriac and abdominal regions in front, and the infrascapular and lumbar regions behind. The arms were uniformly pigmented from the shoulder to the metacarpophalangeal joints. There was an entire absence of pigment over the clavicular and mammary regions in front, and the suprascapular region behind. Scattered here and there through the pigmented areas are patches varying in size from a lentil to a walnut, of clear, pearly skin. The pigmented areas were not raised above the surface, nor were they affected by scraping with the nail or sharp instrument. The thighs and legs were free from pigment. The pigment was more marked over the areolæ and axillary regions. There was evidence of consolidation over the left apex, where there were relative dullness to percussion, diminution of respiratory murmur, some tubularity, and a few dry and moist râles. The lungs were otherwise normal. The symptoms in their order of development were pigmentation of the skin, great weakness accompanied by breathlessness, cough with expectoration, anemia, and, lastly, a tendency to diarrhea. McKendrick (Glasgow Med. Jour., June, 1909).

Case of Addison's disease in a male, aged 31, in whom exposure to the sun darkened the pigmentation, which involved the axillæ, elbows, nipples, breast, the pubis, gums, lips, tongue. Of late the nails have become a dark brown. A. F. Chace (Post-Graduate, Feb., 1911).

Traumatism of the skin is a predisposing cause to pigmentation. The earliest melanodermic patches are often noted to appear over old cicatrices, especially over the healed areas of former blisters, and even the application of a blister or merely of a poultice on an asthenic subject is often sufficient to cause a sudden outburst of pigmentation and permit a positive diagnosis of Addison's disease.

Gastrointestinal disturbances are frequent, but very variable in nature. At the outset, constipation is the rule, and is accompanied by anorexia, which may be accounted for both by the intestinal paresis and by the general lassitude to which we have already alluded. The constipation may be succeeded, particularly in the acute forms, by atonic diarrhea. But the most characteristic symptom is, without doubt, vomiting. Preliminary nausea is very seldom present; the vomiting comes on suddenly, and generally in the morning upon awaking. At first the patient's stomach is evacuated but once a day; then, as the disease progresses, the vomiting becomes more frequent and occurs at intervals during the day. The act takes place with but little muscular effort, of which the subject is, indeed, incapable. The vomitus is colorless, thin, and consists of mucus.

Circulatory disturbances are of great importance. The earlier observers had already pointed out a special weakness of the pulse, together with all the symptoms of cerebral anemia. The researches of Schäfer and Oliver and of Langlois and the later investigations of the action of adrenalin served to direct the attention of clinicians to these disorders, at the same time disclosing their pathogenesis.

The Addisonian subject is in a state of hypotonicity. By reason of the absence or insufficiency of the adrenal secretion, the normal tonus of the vessels is no longer maintained. Even at the outset of the affection, along with the first signs of asthenia, lowered arterial tension is to be found. The sphygmomanometer shows 100 to 120 mm. of mercury. The fall in pressure is accentuated as the disease advances; in the last stages, a tension as low as 50 mm. may be noted.

Bernard and Sergent have brought out a clinical phenomenon which they claim to be useful in diagnosis without the aid of instruments of precision, viz., the "adrenal white line"—as opposed to the red line of meningitis. To cause it to appear, the skin of the abdomen is lightly rubbed with the pulp of a finger, without scratching; after a few moments a rather broad white streak appears, which becomes more and more marked, remains stationary for three to four minutes, then gradually fades off.

Pain and Nervous Disturbances.—Lumbar and abdominal pains of great severity may be present at the outset of the disease. They frequently become localized in the epigastric and hypochondriac regions, and Martineau has described a pathognomonic seat of pain at the anterior extremity of the eleventh rib. These pains, however, almost characteristic when they are sudden in onset, are sometimes entirely wanting throughout the course of the disease.

When considering the pathogenesis of the affection, we shall find it easy to understand how the variations observed in the painful phenomena may be explained according to the extent and the seat of lesions surrounding the adrenals.

We have already mentioned the asthenic manifestations, which, according to us, are referable rather to the muscular system than to the nervous system proper, or at least to the structure which unites the nerve with the muscle—the terminal plate (as formerly designated) or the receptive substance of Langley. True paralyses are rare and in no sense characteristic. Cerebral disturbances, such as the prostration, the tinnitus aurium, the hallucinations, and especially the encephalopathy of Addison's disease, may be due to two causes: cerebral anemia resulting from vascular hypotonicity, and intoxication either through suppression of the antitoxic activity of the adrenals or through the formation of toxic products owing to functional deficiencies—asthenia, hypotonicity, etc.

> Case of Addison's disease with terminal mental symptoms in a woman of 47 years of age, who had been suffering two years from Addison's disease. She became fretful, discouraged, showed diminution of volitional impulses, incapacity for mental effort, and mental defect. She also had ideas apparently dependent upon paresthesia of the skin, *i.e.*, that animals were crawling upon her, that a dog had bitten her upon the arm, that a searchlight was being played upon her back, etc. The patient dying after a sojourn of eighteen days in the hospital, the author was able to make a complete autopsy with microscopical examination. There was healed tuberculosis in the lungs, and the adrenals showed advanced tuberculous degeneration, bacilli being found in the *débris*. H. W. Miller (Amer. Jour. of Insanity, Jan., 1907).

General Disturbances.—The muscular and vascular weakness are necessarily followed by disorders of a general nature. The chemical interchanges are reduced, the phenomena of assimilation greatly retarded, whence result marked wasting of the tissues and a strongly manifested sensation of cold generally accompanied by hypothermia. According to the view of Sajous, who considers Addison's disease as characterized by deficient oxidation and lowered metabolism, a study of the temperature should enable us to judge of the degree of adrenal insufficiency.

The blood in cases of Addison's disease presents nothing peculiar. The search for pigment in the blood-plasma has always proved negative. Generally the blood-cells show diminution, but observations on this subject have been contradictory. While Laignel-Lavastine described diminutions of the corpuscles to three millions, Loeper and Crouzon found a polycythemia. Langlois, in a comparative study of two tuberculous cases presenting similar pulmonary lesions, but one of whom showed distinct Addison's disease, observed no difference either in the hemoglobin percentage, the number of cells or the proportion of leucocytes. The two patients gave identical results.

The secretion of urine is diminished because of the lowered tonicity. Colasanti and Bellati, who made a study of the urine of an Addisonian patient for eighteen days, found its toxicity above that of normal urine. Langlois did not find this abnormal toxicity in the two subjects of which he made a comparative study.

Course and Termination.—Addison's disease always terminates fatally, but its course may be more or less rapid. Sometimes the destruction of the adrenals is so quickly produced that the morbid phenomena show very rapid progression. Asthenia is present almost from the outset, the circulatory disturbances at once become very marked, and, lastly, the gastrointestinal disorders, which do not appear to be closely related to the adrenal insufficiency, may become of such severity, with intractable vomiting and diarrhea, that cachexia and death supervene before the melanodermia has had time to declare itself.

In the cases having a slow course, the disease may remain stationary for a long time, and it is in such cases that are sometimes observed temporary periods of improvement not only with regard to the digestive tract, but also in the symptoms of melanodermia: asthenia and arterial tension. The cause of such periods of improvement it is difficult to state.

We shall lay no stress on the mode of death by progressive cachexia, which presents nothing peculiar, but must dwell with some emphasis upon the form of death which takes place rapidly or even suddenly.

The rapid fatal termination in Addison's disease takes on the features of an acute intoxication. The abdominal pains show marked exacerbation; diarrhea becomes profuse and vomiting continuous, the blood-pressure at the same time showing progressive reduction.

In some cases hypothermia is observed, with a tendency to collapse; in others, on the contrary, there occurs hyperthermia accompanied by delirium and convulsions.

Case of acute Addison's disease in which the duration of the disease was seventeen days. The onset was marked by severe abdominal pain and vomiting. There was, at times, watery diarrhea. Ten days later reddish discoloration of the skin appeared over various points of pressure. These later assumed a more brown color. There was no pigmentation of the mucous membranes. The blood-pressure remained 105 mm. Hg., until the day of the death, when it fell to 99 mm. The clinical diagnosis was malignant tumor of the lungs, pyloric stenosis, and tumor in the right lumbar region. The symptoms, pigmentation, asthenia, psychical disturbance, and sudden death, also suggested Addison's disease. Autopsy showed scirrhous carcinoma of the pylorus with multiple metastases. Both adrenal glands were involved, but only to a very moderate degree. The most striking lesion of the adrenals was a general venous thrombosis, the apparent age of which corresponded well with the duration of the symptoms. The writer believes that the obstruction to venous outflow was the etiological factor in the case. Straub (Deut. Archiv f. klin. Med., Bd. xcvii, S. 67, 1909).

To explain this sudden aggravation in the course of the affection, several hypotheses have been put forth. That one which appears to us the most admissible among them is based on a sudden diminution, sometimes even on almost complete suppression, of the function or rather the functions of the adrenals. Almost always, indeed, such an unfavorable turn in the disease succeeds upon an intercurrent infection. Now, since the researches of Charrin and Langlois, followed by those of Loeper and others, it has been known that certain infections, such as diphtheria and scarlatina, exert a selective action on the adrenal glands, causing

in them a more or less marked functional deficiency. It is thus plain that if in a gland already the seat of tuberculosis, but which, nevertheless, suffices to insure the adrenal function, a fresh lesion appears to destroy the surviving cellular elements the symptoms of adrenal insufficiency will show a sudden outburst and be seen in all their intensity. Boinet has also laid stress on the appearance of serious accidents after excessive fatigue. Such occurrences confirm the investigations of Abelous and Langlois and of Albanèse upon the influence of fatigue on experimentally decapsulated animals.

Another theory accounts for the aggravating effect of intercurrent infections from the fact that, the antitoxic action of the adrenals against certain toxins no longer being exerted, the accidents due to intoxication are more severely manifested. It is evident that this hypothesis explains better than the former the phenomena of excitation, viz., delirium, convulsions, fever.

Sudden death, or at any rate death taking place within a few minutes, is not rare in the bronzed disease, and Addison had already referred to such a termination in his monograph. In 1896 Ihler was able to collect 18 cases, and since that time numerous instances have been noted. Certain cases of sudden death in apparently healthy persons have defied explanation until the autopsy disclosed a tuberculous or cancerous process of the adrenals.

The advent of death may be truly fulminating; a patient previously exhibiting no signs of aggravation in his condition may drop dead while getting out of bed or on attempting to lift a chair. The patient of Dupaigne-Béclère, who was among the first to be treated with relative success by opotherapy, died suddenly in bed during her convalescence. In some cases the end is marked by symptoms of a more striking character, such as a sudden attack of severe vomiting, convulsions, etc. The pulse becomes frequent and thready; the face cyanosed; dyspnea develops, and death occurs.

Accidental syncope, nervous shock, acute intoxication, and sudden adrenal insufficiency have all been advanced as hypotheses in explanation of such occurrences. It is difficult to believe, in this connection, that adrenal insufficiency can produce so rapid an effect, since it is well known that completely decapsulated animals survive for fifteen to eighteen hours and show progressively increasing intensity before death. It appears to us more reasonable to attribute the termination to nervous shock originating in the adrenal or periadrenal sympathetic nerves, and reacting on the general organism with its cardiac and vascular inefficiency resulting from decreased tonic activity on the part of the adrenals.

Case of Addison's disease in a negress, aged 55 years. The face and backs of the hands and fingers were intensely black—much blacker in hue than other parts of the body. The palms of the hands were also abnormally pigmented, but to a lesser degree than the face. There were numerous irregularly defined areas of pigmentation on the mucous membrane of the cheek, gums, and tongue. Her pulse was frequent, small, and regular.

At the necropsy the vagina showed evidence of chronic inflammation of its mucous membrane and presented patches of pigmentation similar in character to those present in the mouth. On the vulva were a few small leucodermic areas. Both suprarenals were enlarged and exhibited caseous masses in their substance,

apparently affecting the cortex. Their capsules were much thickened and adherent to the surrounding parts. They contained caseating masses, at the margin of which were giant cells, in the cortex. The condition was tubercular, with marked tendency to caseation. R. Seheult (Lancet, Aug. 3, 1907).

Three cases of Addisonism occurring in the same family, in sisters, aged 9, 6, and 3½ years, respectively. The father, mother, and an elder sister, aged 19 years, were all healthy. The case of the girl aged 9 years was one of true Addison's disease, with prostration, asthenia, typical pigmentation, low blood-pressure, and occasional vomiting. The other two cases showed only the typical pigmentation and low blood-pressure. Addison's disease is very rare in children under 13 years of age. Croom (Lancet, Feb. 27, 1909).

Clinical Varieties.—Several forms of Addison's disease have been described according to the relative prominence of certain symptoms. These include the gastrointestinal form, painful form, melanodermic form, and asthenic form. These divisions are worthy of acceptance because they correspond in each case to a development and pathogenesis differing from the others. It seems probable, indeed, that in the melanodermic as well as in the painful form sympathetic changes predominate from the outset, while, in the asthenic form, adrenal insufficiency is the primary cause.

Addison's disease in infancy is not rare, occurring in sucklings as well as in later months. Most cases are due to tuberculosis of the adrenals, although some cases have been associated with the perfectly normal glands. The most important symptom is pigmentation of the skin, although pigmentation may be brought about by a long-continued diarrhea in infants. Other symptoms are general depression and extreme weakness, diarrhea and vomiting, and convulsions. The pulse is weak and irregular. The disease is always fatal, dissolution being due to weakness, or to some intercurrent disease, especially tuberculosis. S. Finkelstein (Thèse de Paris, 1900).

Addison's disease in children. Before puberty, *i.e.*, under 13 years, it presents considerable differences from that above this age, and is extremely rare. Analysis of 25 cases, including a personal one. As to relative frequency, Monti found among 200 cases 6 in children below 13, while Greenhow in 330 found it four times; in other words, 1 to 62.

Etiology.—The main etiological factor is tuberculosis, though the patient of Anglade and Jaquin showed no such lesion in the adrenal glands, although extensive tuberculosis in the lungs and spinal cord was present. Age: Twelve cases occurred between the ages of 10 and 13 years, 4 cases between 5 and 10, while 9 occurred below the age of 5. The youngest case on record is that of Belyayeff, of a child 7 days old. Contrary to what textbooks state, that the disease occurs far more frequently in boys than girls, the occurrence in males and females is about equal.

Family History.—Tuberculosis occurred as a family taint in 4 cases; in one instance a rheumatic history; in one instance the mother and four children had had the disease.

Previous History.—In 13 cases in which this was obtained there was tuberculosis of other organs in 3, measles in 2, scarlet fever in 2, tonsillitis and chorea in 1. Felberbaum and Fruchthandler (N. Y. Med. Jour., Aug. 10, 1907).

Hypoglycemia should be included among the symptoms of Addison's disease, as a corollary to the arterial subtension. Bernstein (Berl. klin. Woch., Oct. 2, 1911).

PATHOGENESIS.—The pathogenesis of Addison's disease cannot be explained except by referring to

the data of physiology, and, while Addison was deserving of high credit for pointing out the relation of the bronzed disease to changes in the adrenals, the pathogenesis none the less remained obscure because the functions themselves of the adrenals were still unknown.

Two important theories have been advanced, which, moreover, do not refer exclusively to lesions of the adrenals, but to which recourse is also had to explain the morbid syndromes related to lesions of all ductless glands, including the thyroid gland, the pancreas, etc. These are: 1. The nervous theory, which attempts to explain all the phenomena by an action of the nervous system through its adrenal connections. 2. The glandular theory, which attributes the disturbances to functional alterations in the adrenals.

Nervous Theory. — The nervous theory had already been clearly stated in Addison's second paper, which pointed out the close relations existing between the solar plexus, with the semilunar ganglia, and the adrenals. In France, Jaccoud became a strong partisan and defender of this theory. After him and after Addison, Habershon, Barlow, Schmidt, Mattei, and Martineau attributed the nervous disturbances observed to lesions of the solar plexus and semilunar ganglia. Following Jaccoud, this view is still held by Greenhow, Jurgens, von Kahlden, Lancereaux, Raymond, and Brault. These authors offer as arguments, on the one hand, changes in the adrenals in cases where during life the subject had exhibited none of the symptoms referable to Addison's disease and, on the other hand, the normal condition of the adrenals in individuals declared to have Addison's disease before the autopsy.

Jaccoud supported the theory on the basis of three orders of facts: the symptoms observed, the lesions found *post mortem*, and the structure of the adrenal glands. Among the symptoms observed, leaving the melanodermia out of consideration at once, the nervous disturbances are of two kinds: increasing asthenia and the gastric or nervous manifestations. Prof. Jaccoud, after referring to these symptoms, adds: "If we now bear in mind that in the uncomplicated cases these symptoms show progressive development in the absence of any important visceral lesion, without anemia, without albuminuria, without hemorrhage, and without diarrhea, they will without doubt appear to us as the direct and immediate result of a disturbance of the nervous system." We shall see later that these asthenic phenomena cannot be brought forth as arguments in favor of the nervous theory, and that the capsular theory, as conceived by Abelous and Langlois, itself finds strong support in the asthenia of Addison's disease, described by Jaccoud.

> The autopsy in a case of Addison's disease in a child of 10 years showed tubercular infiltration of the lungs and enlargement of the bronchial glands. The suprarenal capsules were congested, but macroscopically they presented no lesions. A microscopic examination revealed no change in the histological structure. The capsule was of normal thickness, and the gland, as a whole, was not enlarged. The nuclei of the cells were distinct and there was no fatty degeneration. The semilunar plexus was somewhat altered and congested. The mesenteric glands were large, but not caseous. Upon examination the *Bacillus tuberculosis* was absent. Richon (Arch.

de méd. des enfants, tome vi, No. 6, p. 350, 1903).

In every case of true Addison's disease there is a gray degeneration of the nerve-fibers of the splanchnics. This may be either protopathic, when one finds simple atrophy of the adrenals without other inflammatory appearances in these or other organs, or (more commonly) deuteropathic, in consequence of primary disease of the adrenals or pancreas. Withington (Med. News, Sept. 24, 1904).

The attacks of vomiting and the epigastric and lumbar pains are, indeed, in favor of nervous lesions, and it can readily be understood how the close proximity of the sympathetic nervous structures may explain the motor and sensory disturbances observed in cases of bronzed disease. As for the structure of the adrenals, it does not permit of our forming any definite opinion.

While it is quite true that these glands receive a large number of nerve-fibers from the sympathetic, as shown by the researches of Nagel, Bergmann, Kölliker, and Henle, there exist in the cortical layer ganglionic cells which may constitute reflex centers (Moers, Joesten, Holm); and while it is true that excitation of the adrenals tends to inhibit the intestinal movements (Jacob), yet the rôle of the adrenal bodies cannot be denied, even on the ground of their texture alone. The main argument against the pathogenetic rôle of the adrenals is based on the following double series of observed facts: Melanodermia may exist without lesions of the adrenals; marked lesions of the adrenals may exist without melanodermia.

Glandular Theory.—The researches of Brown-Séquard, which followed the monograph of Addison at an interval of but a few months, were steeped in the idea which then prevailed as to the "predominance of melanodermic disturbances in the bronzed disease." Furthermore, while unable to observe pigmentation of the skin in animals deprived of their adrenals, he pointed out the presence of numerous pigmentary granulations in the blood. The most prominent result of his researches, however, lay in the discovery of the functional importance of the adrenals, of which the rôle had until then escaped physiologists. "Death resulting from changes in these organs," wrote this author, "is preceded by a gradually developing weakness, going on to paralysis of the posterior extremities, then of the anterior, and finally of the respiratory muscles. Among the disorders noted may also be mentioned anorexia, failure of digestion, rather frequently delirium, epileptiform disturbances, and a gradual lowering of the temperature." Brown-Séquard concluded that destruction of the adrenals was followed by accumulation in the blood of a toxic substance having the property of becoming transformed into pigment. Since 1855 the investigations on the adrenals have been numerous. The conclusions of Brown-Séquard have been vigorously attacked. Philippeaux, Gratiolet, Harley, Berutti, and Martin-Magron combated the vital rôle of the adrenals, asserting, contrary to the belief of Brown-Séquard, that destruction of these organs did not necessarily result in death.

Tizzoni, in numerous researches carried out between the years 1884 and 1889, likewise recognizes the possibility of survival after destruction of both adrenals; but he points out at

the same time the possibility of regeneration of these organs when not totally destroyed; finally he referred to medullary disorders succeeding upon destruction of one adrenal.

Stirling showed that in a certain number of cases survival after destruction of both adrenals is explained by the presence of accessory adrenals. Alezais and Arnaud ascribed the fatal ending to ascending degeneration reaching the cord by way of the splanchnics.

Clinical and autopsy findings in 3 cases: The morbid changes in the suprarenals were accompanied by corresponding changes in the other glands with an internal secretion, the thyroid, hypophysis, and spleen—all of these were hypertrophied, with evidence of hyperfunctioning. The writer does not regard Addison's disease as due to a single gland, but to several participating in the process. The first symptom in one patient was tremor of the arms, probably the result of professional exposure to electric currents, the man's work being done under an electric light of between 15,000 and 20,000 candlepower. The effect of the Roentgen rays on glandular organs suggests that the light here may have affected the cervical sympathetic, the thyroid, and the hypophysis. Later the process seems to have extended to the abdominal sympathetic and suprarenals. In another case atrophy of the ovaries followed a pregnancy with premature menopause. Calcareous degeneration of the thyroid followed, with tuberculous infection later and fulminating suprarenal symptoms. The diseased suprarenals could not obtain help from the ovaries and thyroid, and there was merely slight hyperfunctioning of the hypophysis as a defensive reaction. In the 3 cases patients in the last stages of Addison's disease recovered their energy and the bronzing subsided under thyroid treatment. The thyroid was already modified and was inadequate to supplant the diseased suprarenals, but it only required slight additional aid from without to be able to counteract temporarily the destructive process in the suprarenals. The disease, the course, the outcome, the histologic findings, the research in the experimental field, all sustain the assumption that Addison's disease, in its complete form, is a general affection of the entire great sympathetic system. Leonardi (Policlinico, Aug., 1909; Jour. Amer. Med. Assoc., Oct. 2, 1909).

In 1891, Abelous and Langlois published their first researches on the functions of the adrenals in frogs; these were followed by a series of papers on the functions of the glands in other animals. They showed that, in all animals subjected to double adrenalectomy, death promptly and inevitably occurs, but that a portion of an organ if left behind is sufficient to cause survival. Muscular weakness and asthenia are all the more intense if the animal be forced to perform muscular movements, whence their first conclusion "that the adrenals possess the function of neutralizing or destroying toxic substances evolved during muscular labor." This conception of the rôle of the adrenals explains a portion of the symptoms observed in Addison's disease, including the most characteristic symptoms: asthenia and the disastrous effects of fatigue.

The discovery of the vasoconstricting action of suprarenal extract by Oliver and Schäfer, on the one hand, and Cybulski, on the other, that of the presence of the active substance in the blood of the capsular vein (Cybulski and Langlois), that of the rapid destruction of this substance in the organism (Langlois), and finally

the isolation of adrenalin by Takamine also threw new light on the symptoms observed. The lowered vascular tension and the cerebral disorders can henceforth be interpreted as resulting from diminution of the tonic influence of the adrenals. The syndrome of adrenal insufficiency in its entirety can henceforth be explained through the data of experimental physiology.

> Study of the nitrogen and sulphur metabolism in a patient who had Addison's disease and who was on a purin-free diet. The desamidating capacity of the patient (capacity to reduce amid nitrogen) and his capacity to transform the sulphur of the cystin group into sulphuric acid were absolutely comparable to that of normal individuals. A considerable degree of acidosis was observed, which is not accounted for by any factor which was found in this examination. The endogenous metabolism of the patient, as represented by the kreatinin and uric acid outputs, was below that of normal subjects. Wolf and Thacher (Arch. of Int. Med., June, 1909).
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> The writer, who had previously observed a striking hypoglycemia after removal of the adrenals, now reports the effect upon the glycogen content of the liver and muscles of the same procedure. Seven dogs were killed at intervals of four and one-half to eight hours after removal of the adrenals. At this time all showed great muscular weakness. Their livers contained an average of 0.722 per cent. glycogen. If one animal be excluded, the average of the other six was 0.222 per cent. Schöndorff found 18.69 to 7.3 per cent. of glycogen in the livers of normal dogs on a similar diet. The muscle content of glycogen was 0.653 per cent., compared with Schöndorff's average of 4 per cent. In three dogs dying spontaneously after operation, the livers contained no glycogen whatever, the muscles an average of 0.187 per cent. The lack of glycogen is the cause of the hypoglycemia. The muscular weakness is, in all probability, due to lack of sufficient sugar and sugar-producing material, for muscle glycogen is well known to be far less readily available for the body than is the liver glycogen. Porges (Zeit. f. klin. med., Bd. lxx, S. 243, 1910).
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> Adrenalin glycosuria is due to the conversion of liver glycogen into sugar. In animals rendered glycogen-free by starvation and strychnine poisoning, adrenalin injections cause a new formation of glycogen and sugar. Pollack (Arch. f. exper. Path. u. Pharmak., Bd. lxi, S. 149, 1909).

Even the insufficiency or complete failure of adrenal opotherapy finds its explanation in the instability of suprarenal extracts. (We retain this vague term to convey the fact that adrenalin is but one of the principles now isolated which are elaborated by the adrenals).

But while physiology can explain and experimentally reproduce most of the symptoms of Addison's disease —those which Bernard and Sergent classify in the syndrome of pure adrenal insufficiency—she has shown herself entirely powerless to reproduce and explain the pigmentation which is so characteristic of this affection.

Excepting in one observation by Boinet, no experimenter has been able to produce pigmentation experimentally, either by destroying the adrenals or by setting up local irritation.

Following Loeper we shall refer into four groups the theories which have been advanced to explain melanodermia: adrenal origin, cachectic origin, nervous origin, and mixed glandular and sympathetic origin.

A. Adrenal Origin.—The elaboration of a pigment by the secretion of

the adrenals, thought of by Brown-Séquard and Pfandler, and which would be caused by lesions of the organ itself, is not supported by any evidence of value. The hemolytic function of the gland and the accumulation in the blood of pigment derived from hemoglobin when the glandular function is weakened are likewise too hypothetical.

B. Cachectic Origin (Gubler, Teissier, Debove).—It is certainly true that any cachexia may provoke, along with general nutritional disorders, pigmentary phenomena. But the bronzed disease is frequently manifest previous to the establishment of cachexia, and presenting features which give it a specific character which does not bear well with the general processes of the cachexia.

C. Nervous Origin.—The intimate connections existing between the adrenals and the sympathetic system are such as to warrant a belief in functional changes in this system during Addison's disease. Addison had already thought of the possible rôle of the nervous system. Jaccoud, Lancereaux, and Raymond defended this theory.

The clinical observations of Semmola and of Brault, who noted melanoderma in conjunction with simple compression of the semilunar ganglia and solar plexus, and the cases of Addison's disease with lesions of but one adrenal (Greenhow) are cited as favoring the view of nervous origin. Irritation of the sympathetic would presumably bring about an overproduction of pigments, either in the blood itself (von Kahlden, Nothnagel), in the chromoblasts (Raymond) or in the cells of the epidermis (Béhier, Chatelin).

D. Mixed Origin.—Attractive as the nervous theory may be, it does not suffice in all cases, and especially is in complete disagreement with experimental facts, since all excitations of the sympathetic, whether extra- or intra- capsular, have proven without effect in producing melanodermia. A number of physicians are at present adopting the opinion of Loeper, that melanodermia is the result of changes both in the adrenals and the nervous network surrounding them. According to Loeper, the adrenal secretion is the normal and necessary exciting agent of the nervous system in its function of regulating pigmentation. Sajous (1903) and Laignel-Lavastine hold an opposite view: the sympathetic is not the regulator of pigmentogenesis, but of the adrenal gland itself, on which the formation of pigment depends.

Addison's disease is not infrequently accompanied by enlargement of the lymphatic glands, and hyperplasia of the spleen and thymus. The writer saw, in one year, three cases of this disease with very marked status lymphaticus. Examinations of the autopsy records of the Berne and Basle Pathological Institutes showed that the latter condition frequently is associated with Addison's disease. The hyperplasia of the lymphatic system in these cases must be due to Addison's disease. By special stains he found that the chromaffin cells of the adrenal gland, including the paraganglion, were greatly reduced. The change or the defective *anlage* of the chromaffin cells is the common cause for Addison's disease and of status lymphaticus. Hedinger (Zeit. f. Pathol.; Charlotte Med. Jour., Aug., 1908).

Two cases, pronounced hypoplasia of the chromaffin system, accompanied the typical Addison's disease, while the lymph-glands were enlarged.

V. Werdt (Berl. klin. Woch., Dec. 26, 1910).

Case of chronic Addison's disease in a youth with the thymolymphatic temperament. The suprarenals had been totally destroyed by a primary tuberculous process, as also in a similar case in a man of 41 with the status lymphaticus. Analysis of these cases and of similar ones in the literature seems to demonstrate a mutual stimulating action between the thyroid and the suprarenals and between the thyroid and the thymus, while there is mutual inhibiting action between the suprarenals and the thymus. Kahn (Virchow's Archiv, June, 1910).

DIAGNOSIS.—The various symptoms encountered in Addison's disease may be divided into two groups:

A. Symptoms of adrenal insufficiency.

Cardiovascular disturbances:—

Lowered arterial tension. Tachycardia.

White line on abdomen.

Cerebral anemia. Syncope.

Disturbances of metabolism:—

Lowered temperature and sensation of cold.

Progressive asthenia. Wasting. Prostration.

Encephalopathy and various nervous disorders. Vomiting and diarrhea.

B. Symptoms of irritation of the adrenal sympathetic.

Melanodermia.

Radiating pains.

Vomiting and diarrhea.

Where the Addisonian syndrome is complete and the course rapid, the diagnosis is easily made. It becomes more difficult when melanodermia is absent or doubtful. A study of the resistance to fatigue, either by means of the ergograph or by simply causing the patient to perform a definite piece of work, combined with the use of the sphygmomanometer, may be of value in facilitating diagnosis, but very often in the hospital, in cachectic tuberculous subjects, the involvement of the adrenals is not discovered till the autopsy.

In fact, the question of diagnosis is generally raised when it becomes necessary to attribute the melanodermic patches to Addison's disease or, on the other hand, to some other affection producing pigmentary changes, such as the pigmentation of cachectic tuberculous cases, pigmentation of hepatic origin, the melanodermias of malaria, arsenic poisoning, lead poisoning, and phthiriasis.

The most common fallacy is to mistake Addison's disease for pernicious anemia; the peculiar lemon tint of the skin in the latter condition, however, is different from that of the characteristic case of Addison's disease; but in slight cases confusion often arises. Fortunately, modern means of examination of the blood, which in Addison's disease is but little abnormal, enable the recognition of the marked blood characteristics of pernicious anemia. The writer, however, cautions against being content with negativing a diagnosis of pernicious anemia because a single blood examination fails to show characteristic changes. The blood in pernicious anemia varies from day to day and from hour to hour. Another possible source of confusion is the discoloration consequent on prolonged administration of arsenic. By inquiry of many persons of considerable experience in arsenical poisoning the writer finds that the occurrence of pigmentation in the mouth is in favor of the case being Addison's disease. In malignant disease the wasting is apt to be much more marked, and local evidence of malignancy can usually be found. Other conditions sometimes confounded with Addison's disease, but which ought to be easily distinguishable, are the filthy, dirty patients, infested with lice, sometimes seen in hospital out-patient departments; phthisical and syphilitic pig-

mentation; Hanot's cirrhosis of the liver, and bronzed diabetes.

Any condition that destroys the functional activity of the medullary part of the suprarenals may cause Addison's disease, by far the most common being tuberculous degeneration. Calmette's reaction helps in this matter. The comparative frequency of malignant disease as a cause, the author considers due to the necessity of having both suprarenals affected, and, perhaps, to the fact that in malignant disease death will be occasioned before the evolution of characteristic phenomena. The proportion of cases in which clinically characteristic Addison's disease has failed to show disease of the suprarenals is so small, about 12 per cent., as to be within the margin of allowable error due to erroneous diagnosis, inefficient post-mortem examination, or the possibility of functional disturbance of the suprarenals. Further, other glands, *e.g.*, the internal carotid and the coccygeal, have cells functionally resembling those of the suprarenals, and it is conceivable that very rarely disease of these glands may cause Addison's disease and lead to death before the suprarenals are affected. On the other hand, when the suprarenals have been found to be diseased, and yet no Addison's disease has been present, it may be that the vicarious activity of these other glands may have formed sufficient internal secretion to prevent the patient having Addison's disease. W. H. White (Clinical Journal, Mar. 18, 1908).

The melanodermia of phthisical patients is all the more likely to lead one astray because of the fact that the cases of Addison's disease are almost all tuberculous. For some authors, moreover, the majority of melanodermic tuberculous cases are cases of Addison's disease in which the adrenal changes are just beginning, not yet showing the signs of glandular insufficiency, but having pericapsular lesions which cause a precocious melanodermia. In pigmented tuberculous subjects without Addison's disease the pigmentation is said to be of a lighter grade and especially the mucous membranes to be unaffected.

Three cases of tuberculosis of the suprarenals in which there was no pigmentation. The diagnosis was made in two from the remarkable weakness of the patients in strong contrast to their well-nourished aspect. Another sign is the low blood-pressure, not to be explained to any disturbances on the part of the heart. Gastrointestinal disturbances without traceable cause are further corroborative testimony. These findings differentiate Addison's disease even without pigmentation of skin or mucosæ. Stursberg (Münch. med. Woch., Bd. liv, Nu. 16, 1907).

Cases of liver cirrhosis and even a few incipient hepatic cases without appreciable change in the size of the liver present either disseminated hepatic patches of discoloration or a diffuse melanodermia of the same color as in Addison's disease. Here again the mucosæ are but slightly or not at all involved, and the hepatic disorders place one on the right track.

Arsenical pigmentation is a rare occurrence; the same is true of saturnine pigmentation. In the latter the blue line on the gums is generally sufficient to permit diagnosis. In pigmentation due to arsenic, the color is more slaty in hue, and a dark mottling is also present, which is rather characteristic. Finally the signs of arsenical intoxication, together with the absence of those of adrenal insufficiency, serve to establish the diagnosis.

In malarial subjects the pigmentation again does not involve the mu-

cous membranes, it is more diffuse and uniform, and the special indications of malaria are present.

The melanodermias of phthiriasic origin (pediculosis) seen among vagabonds in a state of physiological debility, and who are bearers of parasites, are accompanied by itching and cutaneous excoriations. The causative agent may be discovered.

On the whole, it should be borne in mind that the melanodermia of Addison's disease differs from other forms of pigmentation in that it shows marked preference for mucous membranes, although this characteristic should not be put down as absolutely distinctive.

Early diagnosis is all important, though often very difficult. The disease gives rise to definite signs and symptoms, and usually to marked lesions of the medulla of the suprarenal gland. The solar plexus is frequently diseased, owing to the influence of the secretion of the gland in stimulating the sympathetic system. Pathognomonic signs are asthenia, pigmentation, vomiting, and attacks of faintness. If these symptoms are well marked the diagnosis is not difficult, but when they have become evident the chances of successful treatment are not good. Grunbaum (Practitioner, Aug., 1907).

Two personal cases which emphasize the resemblance existing between Addison's disease and tabes dorsalis. Both patients presented an almost identical pigmentation, and both had muscular atrophy. One was a typical case of Addison's disease, while the presence of tabes was undoubted in the other. It is not necessary to assume a combination of tabes dorsalis with Addison's disease, however, since other symptoms of the last-named affection were lacking. The pigmentation should rather be referred to tabetic changes of the nervous system. Possibly the pigmentation in Addison's disease is likewise the expression of disease on the part of the nervous system. In this particular instance atrophy of the shoulder muscles was said to have been present ever since birth, and atrophy of the thigh muscles was claimed to have followed later, in connection with traumatism. Wagner (Berl. klin. Woch., Nu. 15, 1908).

TREATMENT. — Addison's disease of pure type or manifested in the syndrome of adrenal insufficiency without melanodermia is largely caused by tuberculosis of the adrenals. The general treatment of tuberculosis, or rather that form of treatment which is in vogue in a given locality at the time, is indicated. Syphilis of the adrenals is rarely diagnosticated during life; at the autopsy may be found either extensive gummata, a miliary syphilosis or, especially in the young, a sclerosis resulting in atrophy of the gland. In doubtful cases the effect of specific treatment may be tried. Certain cases seem to have been benefited by the **iodides,** with or without the addition of **mercury** (Schwytzer, A. Andrews).

Cases of *bona fide* acute adrenitis with or without hemorrhage, which are almost always frankly infectious in origin (small-pox, diphtheria, etc.), generally run a very rapid course and do not possess any special line of treatment. As for the morbid growths—sarcoma, epithelioma, carcinoma, etc.—which it is almost impossible to diagnosticate during life, unless perhaps it be when persistent edema is noted in combination with the usual syndrome, surgical intervention is indicated, though the results obtained by Israel, Mayo, Kelly, Lecenne, and Hart-

mann have afforded but little encouragement.

Physiological data naturally led to the trial of **adrenal opotherapy.** This treatment was first instituted by Abelous, Charrin, and Langlois in the form of a glycerin extract of the adrenals of guinea-pigs, dogs, and horses. The patients were in such a state of cachexia that no results were obtained, but in two less advanced cases, employing injections each representing Gm. 0.10 of the dried extract, Langlois obtained better results and in particular a notable diminution of the asthenia.

Since that time numerous trials have been made and the treatment markedly altered. Among the methods that have been tried are: 1. Hypodermic injections of the extract. 2. Ingestion of fresh or dried glandular substance. 3. Injection of adrenalin solution. 4. Grafting of adrenal tissue.

1. The injections of extract of the suprarenals were early abandoned because of the great pain they occasioned and the fact that they failed to give satisfactory results in a large number of cases.

2. The ingestion of fresh or dried gland has furnished a few unhoped-for results, together with numerous failures. Béclère and Andérodias report cases of cure, or, perhaps better, disappearance and long-continued absence of the symptoms of adrenal insufficiency. It is advised to use the adrenals of calves and start with doses of Gm. 1.5 to 2.0, which are gradually increased to Gm. 6.0. Sajous employs the dried gland (the glandulæ suprarenales siccæ of the U. S. P.). The dried extract may be given in capsules in the dose of Gm. 0.25 to 0.35 daily for ten successive days; it is left off for four days, then resumed for six to eight days, etc. Systematic testing with the sphygmomanometer should be used as a guide in the treatment. Improvement in the arterial tone is to be considered the sign of efficiency in the treatment, while any indication of hypertonicity demands immediate stoppage of the administration of adrenal.

Adams's paper in the Practitioner for October, 1903, includes an analysis of 97 cases treated with a preparation of the **suprarenal glands.** Of these, 7 were distinctly made worse by the treatment, 43 derived no benefit, 31 showed marked improvement, and 16 were cured. The methods of treatment in these cases may be divided into five heads: 1. Suprarenal grafts. Three patients were treated by this method and all died. 2. Nine patients were treated by fresh glands given by the mouth; of these, 1 became worse, 1 was not benefited, 6 were improved, and 1 permanently relieved. 3. Eleven patients were treated by hypodermic and intramuscular injection. One became worse, 6 derived no benefit, 3 were improved, and 1 permanently benefited. 4. Sixty-one cases were treated with the fluid or solid extract of the suprarenal gland by the mouth. Of these, 2 were made worse, 32 derived no benefit, 17 were markedly improved, and 10 were permanently relieved. 5. Five patients were treated by mixed methods; 3 were improved and 2 cured.

The cases most likely to derive benefit from the specific treatment are those in which the process is a chronic sclerosis and in which the other organs are fairly sound. D. Symmers (Med. News, Sept. 10, 1904).

Case of Addison's disease which improved remarkably under the **open-air** treatment and the simultaneous administration of **suprarenal extract.** The patient, a man, aged 36, had been ill for eighteen months. He applied for

treatment early in November, the weather at the time being cold, wet, and stormy. The man was placed on the balcony outside the hospital ward and stood the exposure well. The suprarenal extract was administered in 5-grain doses three times daily. All the symptoms disappeared rapidly and the patient was discharged as cured five and one-half months after the beginning of the treatment. Death occurred suddenly two years afterward, due to asthenia and failure of the heart action. Bramwell (Brit. Med. Jour., Oct. 28, 1905).

Case in a male, aged 18, which followed a very rapid course, *i.e.*, less than four months, although suprarenal gland was given up to 15 grains thrice daily. At the autopsy chronic adrenal tuberculosis was evident, with secondary inflammation of the neighboring sympathetic plexuses. Second case in a female, aged 32, who had been ill two years. **Adrenal gland** caused so much improvement that she stood pregnancy parturition easily, and bore a healthy child. She was given 5 grains, which were rapidly increased to 20 grains thrice daily. If she vomited the adrenal extract for a few days her symptoms began to return. A. G. Gullan (Lancet, Aug. 19, 1905).

Case reported in a boy 18 years of age, who was brought to the hospital in a fainting condition. He was gasping for breath and sank exhausted into a chair. A walk of half a mile preceding his admission was accomplished with the greatest difficulty, and only after repeated rests. The pulse was uncountable; respiration was rapid. The symptoms had existed for three months. It was stated by the mother of the patient that the boy's father had died of the same disease after some years of illness. The skin was generally pigmented, with well-marked patches on the forehead. The patient only complained of extreme fatigue. After a few days **extract of suprarenal** was administered in the form of tablets, beginning with 1 three times a day, which soon increased to 2 three times a day. Under the treatment improvement was rapid. In two weeks there was a gain of 6 pounds in weight and the pulse had decreased to 110, and he was able to move about the room with less difficulty. The pigmentation was less marked. The treatment was continued until 500 tablets were taken. The patient gained 56 pounds in weight, the pigmentation entirely disappeared, and he was able to resume work as an active farm laborer. R. E. Weigall (Austral. Med. Gaz., Oct. 20, 1905).

The writer takes the blood-pressure at least three times in all suspected cases, and if it is found low administers **suprarenal extract** by the mouth, 3 grains three times a day, for three days. If there is a rise of more than 10 per cent. in the pressure, the probability that the patient suffers from adrenal insufficiency approaches a certainty. In regard to the blood, the opsonic index of the serum for the tubercle bacillus may be taken, as tuberculosis is the commonest cause of the destruction of the capsule. Grünbaum (Practitioner, Aug., 1907).

Case of Addison's disease which exhibited all the typical symptoms of this affection. When the patient was first seen the adynamia was so marked that an unfavorable prognosis was made. Owing to the secretory and motor insufficiency of the stomach, **gastric lavage** with **salt solution** was practised. **Nutrient enemas** were given and **hydrochloric acid**, but nothing else in the way of remedial agents. The patient slowly gained in strength and weight and eventually was dismissed in a very much improved condition. The skin pigmentation also lessened, but not so much but that a military surgeon was able to diagnose Addison's disease when the applicant was examined for the service. Since 1903 the patient had improved steadily, and the author believes that the man may be considered as cured. In another instance, to which reference is made, this treatment produced similar good results. The importance of gastric lavage is emphasized in these and other cases for the purpose of removing from the gastrointestinal canal toxins which it may

contain. Grawitz (Deut. med. Woch., July 4, 1907).

Our experience with Addison's disease justifies the belief that one-sixth of the cases can be cured by the timely and persistent use of **suprarenal extract**, while a considerable larger proportion, perhaps 25 per cent. more, can be substantially benefited. It does not appear that surgery can help us here, because in so far as the adrenals are involved it is the loss of secretion, as it is of the thyroid in myxedema, which lies at the bottom of the syndrome. G. W. McCaskey (Jour. Indiana State Med. Assoc., Jan. 15, 1908).

Case of well-defined Addison's disease in which the extreme languor, asthenia, and emaciation indicated a rapidly fatal outcome, but under **organotherapy** the symptoms subsided and the patient, a man of 34, has been in good health during the ten years since. The gland substance was eaten fresh and a glycerin extract was injected two or three times a week. There are still traces of pigmentation, confirming, the writer thinks, the assumption of the nervous origin of this symptom. Béclère has reported a similar case of permanent recovery under organotherapy. The suprarenal treatment evidently acts by stimulating to hypertrophy the parts of the suprarenal capsules which are still intact, thus insuring adequate functioning. The writer cites 5 other cases that have been reported in France with marked improvement under organotherapy and adds 3 from his own experience, all the symptoms, except the pigmentation, showing great benefit from the **suprarenal treatment.** E. Boinet (Bull. de l'Acad. de Méd., Oct. 5, 1909).

Series of 120 cases collected from literature, including 97 previously collected by E. W. Adams, in all of which **adrenal preparations** had been used in some form, gave the following results:

1. Cases in which death can be ascribed to grafting or adrenal preparations 8
2. Cases in which the benefit was slight or *nil* 51
3. Cases in which marked improvement occurred 36
4. Cases in which permanent benefit was obtained 25

120

Analysis of these cases shows that far better results could be obtained by a careful adjustment of the dosage to the actual needs of each individual case. Addison's disease being due, from the writer's viewpoint, to inadequate oxygenation and metabolic activity, the result in turn of a deficient production of the adrenal secretion, it follows that *the temperature and blood-pressure indicate the degree to which the adrenals are still performing their functions.* It is plain, therefore, that our aim should be *to supply only just enough adrenal extractive to compensate for the deficiency of adrenal secretion produced.*

The 25 cases of Addison's disease in which, out of the 120 referred to above, permanent benefit occurred include one, treated by Bate, in which but 1/12 grain (0.005 Gm.) of **adrenal extract** three times daily caused very great and lasting improvement with marked lessening of the bronzing. When the remedy could not be obtained temporarily, which occurred twice, the case relapsed. On the other hand, Suckling began with 10 grains daily and gradually increased until 175 grains were given each day, and also obtained favorable results. That in Bate's case the adrenals were still able almost to carry on their function is self-evident, while in Suckling's the remedy practically compensated for the adrenals (while the local morbid process in them was still active, and such as to paralyze their functions—a fact well shown by the severity of the case when the use of the extract was begun). The average dose is probably that used by Weigall in a very severe case—5 grains, increased to 10 grains, of the extract three times a day. The patient increased 6 pounds in two weeks, and after about three months 56 pounds. In other words, in the 25 cases of permanent benefit, although the remedy was used empirically, it so happened in all probability that *the*

doses employed coincided with the needs of the organism. In the 51 cases in which no benefit was obtained several occur in which failure was evidently due to inadequate dosage or to too early cessation of the treatment, while in others excessive doses—practically in every instance a too rapid or excessive increase of the dose—as clearly prevented a successful issue. Sajous (Monthly Cyclo., April, 1909).

3. The injection of **adrenalin** recommended by Netter and Sergent appears to us best suited for the cases showing low arterial tension, whether of adrenal origin or not.

4. **Grafting of adrenal tissue.** The only rational treatment for adrenal insufficiency is grafting of the gland. Experimentation shows, indeed, that the substances secreted by the gland are very quickly destroyed in the organism, and that either the ingestion or injection of the extract can, therefore, produce but very evanescent effects, which, besides, cannot completely replace the activities as yet unknown having their seat in the glandular cells themselves. Unfortunately, success in adrenal grafting is not easily obtained, and in cases where the vitality of the grafted gland has manifested itself accidents of so grave a nature have been noted that grafting has been considered an impracticable method. Courmont reports 3 cases of the grafting of dogs' adrenals in man and states that in all of them the results were disastrous. His personal case developed a formidable hyperthermia and cardiac collapse.

Sajous has collected from the general literature 120 cases of Addison's disease treated by opotherapy in its various forms and presents the following table:—

1. Cases in which death can be ascribed to grafting or adrenal preparations	8
2. Cases in which benefit was slight or *nil*	51
3. Cases in which marked improvement occurred	36
4. Cases in which permanent benefit was obtained	25
	120

Thus, **adrenal opotherapy,** while it remains the rational mode of treatment in Addison's disease, requires that the subject be kept constantly under supervision. It cannot, therefore, be considered a harmless form of medication.

J. P. Langlois,
Paris.

ADENITIS.— DEFINITION. — Inflammation of a gland.

VARIETIES. — Adenitis may be *acute,* due almost invariably to infection from an attack of angioleucitis and occasionally to injury or strains; or *chronic,* resulting from either of the preceding, especially in strumous or cachectic persons, and from slight sources of irritation, and not uncommonly resulting in permanent enlargement and induration or in tuberculous degeneration. Adenitis of specific origin will be described under Syphilis and Urinary System.

ACUTE ADENITIS.

SYMPTOMS.—The general symptoms depend upon the extent and severity of the infection. Rigors may occur when pus forms. The temperature is frequently elevated. If the infection is severe, symptoms of profound septicemia appear.

The local symptoms are, by far, the most prominent in the majority of cases, and consist of pain, heat, and swelling. The suffering varies from a slight soreness only to intense pain according to

the position of the gland, its relations with the surrounding tissues, and the density of the tissue in which it is imbedded. The heat may vary according to the degree of the congestion present. The swelling may either be great or slight. If the lesion be confined to the gland, it will be well defined; if periadenitis is present, the swelling will be more or less diffuse. Glands in any region of the body may be affected, but those of the neck, axilla, and groin more than the others; this is due to the fact that infection generally enters the system through the mouth, throat, genital organs, and the extremities.

In the congestive, or exudative, stage, pain and swelling are present in the region of the glands; if the glands are superficial the swelling is ovoid, with the long axis coinciding with the direction of the afferent lymphatics, and palpation reveals several movable, hard, elastic, and tender rounded masses.

When the glands are deep, as in the axilla, abdomen, or even the neck, the results of palpation are less definite and unsatisfactory.

In the suppurative stage the pain increases and becomes sharp and catching, the skin reddens, and the periglandular tissue swells.

If the gland alone suppurates, the skin remains normal, while under it may be felt the softened and enlarged gland. This latter opens outwardly or into the neighboring cellular tissue on from the sixth to the fifteenth day of the affection. When the gland opens outwardly, the cicatrix is much smaller than when it ruptures into the cellular tissue, as in the latter case it gives rise to an abscess.

If the cellular tissue around the gland suppurates, the skin becomes quite hot, swollen, and painful, and fluctuation may be felt. Two foci of suppuration are thus established. The skin is occasionally undermined by the pus. Recovery is possible, however, without suppuration of the gland.

Both the gland and the cellular tissue around it may suppurate, either simultaneously, or suppuration of the cellular tissue may precede that of the glands, or the latter may suppurate and rupture into the surrounding cellular tissue and form an abscess. Pus is usually produced in considerable quantity, and the affection is of long duration.

Suppurative adenitis may result in cicatrization after several weeks. This cicatrix may reopen to allow the exit of pus from a suppurated gland. On the other hand, a fistula may result, which may give exit to seropus or to lymph (Desprès). A lymphatic gland or vessel will then be found at the bottom of the abscess cavity, below the crater-like opening.

As the suppuration usually starts in more than one focus in the gland, the first sensation to the touch will be one of bogginess, which periglandular congestion may render obscure. Well-defined fluctuation is found only when considerable tissue is destroyed.

> The writer reports the case of a child that had been referred to him with the diagnosis of hypertrophy of the thymus gland, the chief symptoms being dyspnea and retrosternal dullness. On operating with the intention of removing the thymus this organ was found too small to account for the symptoms, but deeply behind the sternum, between the innominate artery and the trachea, the author came upon a grayish mass, which proved to be a suppurating lymph-gland. This and another large node situated at the side of the trachea were removed. The result was satisfactory, the suffocative attacks being relieved. The lesson drawn from this

case by the author is that predominance of abdominal recession during inspiration, as against almost complete absence of suprasternal and subclavicular recession, as had been previously noted in this case, is a point of considerable importance in the differentiation of mediastinal periadenitis from thymus enlargement. Veau (Bulletin méd., Mar. 1, 1911).

DIAGNOSIS.—The diagnosis of ordinary superficial acute adenitis is usually easy; it is more difficult when the neighboring cellular tissue is also inflamed; it may be impossible in cases of deep-seated or visceral adenitis.

In adenitis of the inguinocrural region the swelling is found in the external portion of the region if due to a lesion of the gluteal tissues, and in the inner portion of the region if due to a lesion of the anus, perineum, or external genitals. In both conditions the tumor will have its long axis directed more or less horizontally.

The swelling will be found in the lower portion of the inguinocrural region, with the long axis directed more or less vertically, if the lesion causing it is situated on the foot, leg, or lower part of the thigh. This disposition is due to the anatomical relations of the lymphatic vessels and glands, and should be borne in mind. Operation for strangulated crural (femoral) hernia has been performed for an adenophlegmon of the crural canal.

Supraclavicular adenitis, while frequent in phthisis, is not present in every case. Yet it is of great diagnostic value when present. There may be a few or a great number of slightly enlarged glands, and they are frequently bilateral. The cervical glands may also be enlarged. There is no pain, nor does the swelling increase, remaining just the same for years. They rarely accompany apical tuberculosis, but are generally found with peripheral, subpleural lesions. The writer considers that the presence of enlarged supraclavicular glands confirms the diagnosis of doubtful phthisis. C. Sabourin (Jour. des praticiens, Dec. 27, 1902).

New sign described, based on auscultation at level of seventh cervical or first dorsal vertebra. When the child speaks in a low voice the voice sound is accompanied by an added whispering sound, localized to one or two vertebræ, or extending even to fourth or fifth dorsal vertebra. It is present long before dullness appears. The bronchial quality of respiration over this area is also significant, but it only appears when the glands are considerably enlarged. The absence of abnormal breath sounds and apical râles affords corroborative evidence. D'Espine (Brit. Med. Jour., Oct. 15, 1910).

ETIOLOGY.—The lymphatic glands serve as reservoirs on the course of the lymphatic vessels, through which any irritants or infection must pass.

Cold and overexertion act as local depressants, and thus may indirectly favor the development of adenitis. General debility has the same effect. The following varieties of adenitis, etiologically regarded, are recognized:—

1. Adenitis by contiguity, resulting from the propagation, by contact, of a neighboring inflammation.

2. Adenitis by continuity or following lymphangitis.

3. Adenitis by embolism, due to the transportation of septic or irritating matter, produced in the system or coming from the outside.

Adenitis of the mesenteric glands may be due to dysentery or to the inflammation of Peyer's patches in typhoid fever.

Adenitis occurs in carbuncle, furuncle, vaccination, erysipelas, and eruptive or infectious fevers.

Attention has been called by many

observers to the frequent association of enlargement of the cervical glands and diseased tonsils. So often has this been found that every patient suffering from cervical adenitis should have the tonsils examined, with a view to their removal if diseased. The contents of the tonsillar crypts should be examined microscopically, and the identity of the bacterial growths therein ascertained. It is wise to submit the tonsillar mass to bactericidal measures—iodine in glycerin, for example—sometime before removing them.

> The ordinary operation of tonsillectomy removes only the protruding portion of the tonsil. The submerged tonsil, which frequently extends a distance of one-half to three-fourths of an inch into the tissues of the neck, is the one that gives the most trouble, and is the one that is the most difficult to remove. No single instrument can be relied upon for the removal of this tissue. If the tonsil is situated so that it can be drawn out by forceps, the old guillotine can be used, but this only applies to a limited number of cases. Usually the tonsil must be grasped with forceps and carefully cut loose from its capsular sheath, after which it is removed by the wire snare or guillotine. A tonsillar curette is valuable for removing the masses at the bottom of the cavities which have been left after the snare or punch forceps. The tonsil may be drawn from its bed by a thread, which is found often more useful than the forceps, as it does not need readjusting in cases of bleeding or vomiting. As a rule the operation can be done without general anesthesia. In every case of enlargement of the lymph-glands the tonsils should be thoroughly removed. R. C. Myles (Jour. Amer. Med. Assoc., Oct. 29, 1904).
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> The writer made histological examinations of 65 whole tonsils removed from children; 57 tonsils of patients not clinically tuberculous showed no tuberculous lesions. Of eight patients with tuberculous cervical adenitis the tonsils were found tuberculous in five. In two of the cases there was evidence of other than tonsillar source for the tuberculous infection. F. S. Matthews (Annals of Surg., Dec., 1910).

PATHOLOGY. — If suppuration does not occur, resolution may take place, or chronic enlargement of the gland may follow hyperplasia of the connective-tissue stroma of the gland.

If suppuration does occur the surrounding connective tissue may, and usually does, suppurate; then the more or less disintegrated gland lies in a suppurating cavity formed by the circumjacent connective tissue.

There are two forms of acute adenitis, depending upon the degree of inflammation present:—

1. Exudative adenitis. In this form the gland is swollen, and it feels hard and elastic. On section it appears reddish brown, like the spleen, with small foci of hemorrhage, all of which indicate excessive dilatation of the capillaries. The lymphatic stream is arrested by the dilatation of the cortical lymph-sinuses and their obstruction by fibrin, granular material, and portions of altered white corpuscles. The lymph-follicles are filled with fibrin and accumulated lymph-cells. The stroma of the gland is swollen and infiltrated with cells.

If the section of the gland is scraped, a milky liquid will be obtained, which contains white corpuscles and epithelial cells, the latter showing several nuclei.

2. Suppurative adenitis. In this variety the gland softens, its tissues become more brittle, hemorrhagic infiltration centers form that soon change into yellow, purulent foci. These, at first distinctly separate, soon unite, forming an abscess within the fibrous capsule of the gland. Sometimes the

periglandular tissue suppurates, while the gland does not.

The glandular abscess and the periglandular abscess may open externally, each one separately or both simultaneously. The suppurating gland may rupture into the cellular tissue. Occasionally the gland is hard and elastic; it may be difficult to separate it from its fibrous capsule. The afferent lymphatics are enlarged and thickened. The lymph-cells and cortical follicles are few in number and have undergone granulofatty degeneration.

PROGNOSIS.—The prognosis is usually favorable; it may be unfavorable, however, when extensive abscesses form in the neighborhood of important organs.

Deep-seated suppurative adenitis may give rise to dangerous complications, especially in certain regions, like the neck and mediastinum, on account of the purulent extensions (through burrowing) and the difficulty of evacuating the pus.

Ulceration of the great vessels of the neck giving rise to grave hemorrhages may also occur.

TREATMENT.—The first indication in acute adenitis is to **remove any source of irritation or infection.** Any wound, abrasion, opening, or any natural cavity with which either of these may connect should be so treated as to bring about absolute **local asepsis.**

> Enlarged glands of the neck are not, primarily, tubercular, and bear the slightest relation, if any, to general or pulmonary tuberculosis. They are due to a mixed infection of pus-producing bacilli, and will quickly resolve if the source of the infection is removed before the glandular tissue becomes disorganized. If disorganization takes place, the gland should be **poulticed** until it is practically liquefied. It should then be **opened** by a stab puncture, **emptied** and **drained** by a Briggs cannula. Cases seen late with a large mass of partially calcified and partially disorganized glands present call for a thorough and extensive dissection. Treatment, other than local, should be **food, fresh air,** and **proper clothing.** F. D. Donoghue (Boston Med. and Surg. Jour., Mar. 28, 1907).

The region in which the affected gland is situated should be kept at rest and, if possible, elevated. In this manner the afferent arterial current is diminished, while the efferent venous and lymphatic currents are increased.

To prevent suppuration, **gray mercurial ointment,** very gently rubbed in, is useful. The injections of from 5 to 10 minims of a 3 per cent. **carbolic acid solution** into an inflamed gland have also proven satisfactory.

If it is desired to hasten suppuration, warm **antiseptic fomentations** are to be used in preference to poultices. The **compound resin cerate** of the pharmacopœia is effective for this purpose, and is antiseptic as well.

When pus has formed, the gland should be opened by a generous **incision,** sinuses, if present, being opened throughout their entire length to facilitate treatment. The **contents** are then carefully **removed,** and the infiltrated **wall scraped** with a sharp curette. The cavity should then be **packed with iodoform gauze,** or **gauze impregnated with camphorated naphthol** or **salol.** The dressing may be removed on the third day.

> Sufficient attention has not been paid to the subject of wholly avoiding or at at least minimizing the scar in the surgical treatment of cervical adenitis. Many cases of cervical adenitis occur in which this is of great importance, and in which radical operative measures are not demanded. In such cases **aspiration,** or the use of a **seton, or** both, while not infallible, may prove

successful. When the tuberculous glands do not subside under medical treatment, **excision,** done with extreme care and reasonably early, is the method of choice. Neither aspiration nor the use of a seton should be resorted to in cases involving the deep cervical glands. Bulkley (Amer. Med., Feb. 27, 1904).

In addition to **climatic and** general **tonic treatment,** the writer advised the **evacuation** by puncture of suppurative adenitis and the injection of a mixture of **iodoform,** 1 part; **ether,** 10 parts; **oil of sweet almonds,** 100 parts; **creosote,** 2 parts. In chronic cases cure may be obtained in two or three months after about twenty punctures. Robin (Tribune méd., xli, 249, 1908).

Balsam of Peru is a valuable curative agent, as it is not only antiseptic, but is a stimulant to healthy granulation. It is applied directly to the open, cleansed wound, and then covered with gauze and retaining bandage.

In the treatment of cases of simple chronic adenitis, applications of **iodine, compression,** and **local blistering** have given the best results.

Blisters, **nitrate of silver,** or iodine tincture should be applied around, but not over, the inflamed gland.

Excision may be performed if the mass be large or disfiguring.

In cervical adenitis due to tonsillar infection some authors have strongly advised the thorough **removal of the diseased tonsil** before attempting the external operation upon the glands, especially in those cases in which the lymph-glands have not broken down. The extension of the infection through the lymphatics from the tonsils is thus checked.

In cervical adenitis due to tonsillar infection, the writer removes the diseased tonsil itself before attempting the external operation, in cases where the lymph-glands have not broken down. The cervical glands receive their lymphatics from the tonsils, and the extension of the infection, a common occurrence, is thus checked. Five cases reported in which the neck swelling disappeared after **removal of the diseased tonsillar tissue.** Some of these cases had advanced to a considerable involvement of the cervical glands. A. E. Rogars (Med. Rec., Nov. 28, 1903).

Electricity, preferably the constant current, is highly recommended by some authors. Daily sittings of ten minutes each, using 5 to 15 milliampères, are required.

Codliver oil, the **iodides,** and **iron** are indicated in all cases when the digestive organs do not rebel against their use. **Arsenic** and **strychnine** are the agents next in order, and sometimes prove very effective. **Out-of-door life** and plentiful **nourishment** are of primary importance.

CHRONIC ADENITIS.

SYMPTOMS.—The symptoms vary according to the period of development in which the diseased gland is found at the time of examination.

Three periods of development are commonly recognized in tuberculous adenitis: the period of induration, or indolence; the period of inflammation, and the period of suppuration.

1. Period of Induration, or Indolence.—This period may last for years, and resolution may even take place, though the gland always remains somewhat enlarged and indurated. The glands are felt as hard, elastic, enlarged bodies, rolling under the finger, with more or less distinctness as they are situated superficially or deep. No heat, pain, or redness of the skin is perceived.

2. Period of Inflammation.—In this period we have pain, redness of the skin, and tenderness on pressure. The gland, if solitary, may adhere to the skin. Fluctuation may be present.

3. Period of Suppuration.—In this period we notice much more softening of the contents of the gland than a real suppuration. The skin may ulcerate through almost without inflammatory symptoms, and the contents—consisting of caseous matter half-dissolved in a whitish watery fluid—may be evacuated. When periadenitis occurs, true pus may be present.

If chains of glands are tuberculous, the latter inflame alternately and discharge their contents in the same order, a series of abscesses being thus formed.

When the contents of the gland are discharged, the skin may become ulcerated in the neighborhood, form fistulæ, and after healing leave a depressed, adherent, violet-colored cicatrix.

In some cases a fistula may form and last for years; the skin may be undermined, and disfiguring cicatrices may be formed.

Cretaceous transformation occurs at times in the deeper glands, but rarely in the superficial ones. Some caseous glands undergo a process which transforms them into a cyst-like cavity containing a serous liquid.

In chronic adenitis the glands may become painful by the compression of small nerves, or of neighboring organs; when they are inflamed a small, hard mass usually appears, either alone or united with others, which may become enlarged and suppurate, or persist with practically no change for years, or finally disappear if the cause of irritation be removed.

Chronic adenitis may assume various forms.

1. General Tuberculous Adenitis.—This presents itself especially in negroes. Organs other than the glands are but little affected, and continuous fever exists. The retroperitoneal, bronchial, and mesenteric glands are the most enlarged. It resembles in many ways an acute attack of Hodgkin's disease.

> The majority of children presenting symptoms of tuberculosis also have general adenitis, the swollen glands being felt everywhere; they never change in size or consistence. Suddenly a bronchitis develops, followed by a bronchopneumonia, from which the child dies. Microscopical examination reveals caseous spots and the presence of tubercle bacilli throughout the affected glands. The name of "generalized peripheral adenitis" is suggested for this condition. Grancher and Marinescu (L'Union Méd., Dec. 2, 1890).

2. Local Tuberculous Adenitis.—(*a*) Cervical. This form is usually met with in children, and begins in the submaxillary glands, which are generally more enlarged on one side.

(*b*) Bronchial. This form is thought to be always secondary to a focus in the lungs, by some authors, but this opinion is contested by many others, Osler among them. Local lung infection, pericardial infection, and general infection are to be feared, however.

(*c*) Peribronchial. In this form we must realize the importance of lesions resulting from caseation. There is a softening of the lymphatic glands situated around the lower end of the trachea and main bronchi. Evidence from percussion is of doubtful value; alterations in breath-sounds are much more important, especially when unilateral; divided respiration, with prolonged expiration, is found unaccompanied by any adventitious sounds. In cases in which the enlarged glands ulcerate through the air-tubes, the breath has a very offensive odor, and coexistence of fetor with hemoptysis and evidence of pulmonary consolidation is suggestive. When vomiting of

blood and its passage by the bowel are added, the diagnosis of glands rupturing into the bronchus and esophagus is the most likely one.

General tuberculous adenitis is likely to occur in such cases unless prompt remedial measures are instituted.

(*d*) Mesenteric. This form may be primary, and is thus very common in children, or secondary to local intestinal tuberculosis. The sufferers are usually weak and wasted; the abdomen is enlarged and tympanitic, and diarrhea is a common symptom. Some fever is usually present. This form may exist in adults.

> Sims Woodhead found tuberculous mesenteric glands in 78.7 per cent. of necropsies on tuberculous children, and in 11 per cent. the mesenteric was the only lesion present. Colman found them in 66 per cent. of the necropsies; Walter Carr in 54 per cent.; W. P. S. Branson in 22 per cent. When this condition is present in adults, it is found to affect most frequently the glands of the appendix, or of the ileocecal region, because, according to Corner:—
>
> 1. The cecum is like the stomach, a resting place for the bowel contents in its passage.
>
> 2. The bowel contents contains a maximum number of organisms in the cecum.
>
> 3. The lymphoid tissue has its greatest development in the ileum, the cecum, and especially the appendix. Louis Rassieur (Jour. Missouri State Med. Assoc., Feb., 1909).

DIAGNOSIS.—Chronic adenitis is generally limited to one or two glands; when the glands are tuberculous, chronic adenitis is apt to affect an entire mass. The former is often associated with an external simple lesion; the tuberculous form is apt to be more frequent in children, young soldiers, and negroes.

A fragment of the suspected tissue may be implanted into the subcutaneous connective tissue of the groin of a guinea-pig, and if the specimen is tuberculous a miliary tuberculosis will develop in from five to six weeks.

The use of the tuberculin test in the diagnosis of tuberculous adenitis is reliable and harmless. The tuberculin used is a 1 per cent. solution of Koch's original product, from 1 to 5 mg. constituting a usual dose.

If in from six to twenty-four hours after the injection of tuberculin solution there occur weakness, sensations of heat and cold, general malaise, nausea, anorexia, severe headache, pain in the back and limbs, and if these symptoms are sharply defined in both their beginning and ending, reaction is considered to have occurred.

Supraclavicular adenitis, while frequent in phthisis, is not present in every case. It is, however, of great diagnostic value when present. There may be few or many slightly enlarged glands, and they are frequently bilateral.

Lymphadenoma.—This variety of tumor is usually more voluminous and is not suppurative. The diagnosis, however, is exceedingly difficult.

Simple Adenitis.—This is an acute affection usually ending in a few days in suppuration.

Syphilitic Adenitis.—When a primary sore is present, numerous, small, hard, indolent glands can be felt if the region is supplied with a chain of lymphatics. When in secondary syphilis there is glandular enlargement, a large number of external lymphatics take part in the process.

Carcinoma.—The enlarged glands are small and hard, and can generally be distinctly traced to the growth.

Lymphosarcoma. — This persists

longer and is much larger before degeneration occurs.

Chronic adenitis is frequently a complication of malignant tumors. Supraclavicular adenitis appearing during the course of visceral cancer is usually situated on the left side (found 27 times on that side by one author). It may be solitary or accompanied by adenitis in other regions; it usually appears late and develops rather rapidly. When occurring early it may be very useful for diagnostic purposes.

From a clinical point of view this adenitis may be known by its ligneous hardness, its painlessness, its freedom from adhesions, and by the union into one solid mass of all the glands forming it.

ETIOLOGY.—This form of adenitis frequently follows some neighboring superficial lesion, such as eczema, impetigo, conjunctivitis, or the exanthemata. Catarrhal inflammation of the mucous membranes predisposes to tuberculosis of the glands. The resistance of the lymph-tissue is weakened. This explains the frequent development of tuberculous bronchial adenitis after whooping-cough and measles, and of mesenteric adenitis in children with intestinal disturbances.

Cervical adenitis is not a manifestation of an already generalized tuberculosis; the bacillus penetrates, by solution of continuity of the mucous membranes or the skin, to the ganglion, which becomes a seat of infection (Duhamel).

Enlarged glands of the neck are not, primarily, tubercular, and bear the slightest relation, if any, to general or pulmonary tuberculosis. They are due to a mixed infection of pus-producing bacilli, and will quickly resolve if the source of the infection is removed before the glandular tissue becomes disorganized.

A distinction should be made between hereditary (congenital) and acquired tuberculosis. In the latter case the author's views seem rational and correct, being comparable with and analogous to the phenomena observed in carcinoma and syphilis. When the infection is acquired there is, at first, a local seat, or focus, of infection in which the disease germs develop and from which, after proliferation, they spread until the disease becomes more or less generalized,—the germs being transmitted through the lymphatic system to the lungs and thence in the blood-stream to the various organs of the body; the various glands along the course or path of transmission become affected and in turn become additional possible foci of infection. On the other hand, when the trouble is hereditary the glandular manifestation is an indication of an already generalized tuberculosis.

Youth predisposes to caseous adenitis on account of the predominance at that period of the lymphatic system. Crowding, humidity, and bad or insufficient food are also predisposing factors. Tuberculous adenitis is frequently observed in temperate regions. Negroes brought to such climates are especially prone to become sufferers.

The absorbent power of the lymphatic system is so great that the morbific principle of tuberculosis may be transported to the glands without visible external lesion of the skin or mucous membrane.

Axillary adenitis is frequently secondary to chronic tubercular lesions of the lungs (Lépine).

The cervical glands are occasionally found affected in phthisical patients.

Observations by Mitchell, of Johns Hopkins Hospital, upon 170 cases of tuberculous cervical adenitis show the disease to be more prevalent among negroes than among whites, males preponderating over females in the proportion of 3 to 2, the majority being between 10 and 30 years of age. A family history of tuberculosis was present in about half the cases, though only 4 per cent. showed positive evidence of the disease in the lungs. The condition is regarded as a local manifestation of infection through the tonsils, adenoids, or carious teeth.

PATHOLOGY.—Usually an entire group of glands is affected. The glands are isolated when the irritation and rapidity of growth are not great; this usually occurs in secondary visceral adenitis. In other cases—especially when the glands are superficial, where the adenitis is primary—the glands are united into a large lobulated and irregular mass, the size of which may vary from that of a small nut to that of an orange.

If the adenitis follows a visceral tuberculosis the afferent lymphatics show, in some cases, signs of tuberculosis, as is the case in pulmonary and mesenteric tuberculous meningitis.

Two varieties of lesions are to be noted: 1. Lesions of chronic adenitis affecting the stroma and the elements of the gland, which becomes hypertrophied. 2. Specific lesions of tuberculosis, consisting in miliary granulation at first, ending in caseation. As one or the other of these two processes is the more prominent, so will the lesion vary in appearance. Deep adenitis is never so sclerous as the superficial variety, the latter being characterized by a more vigorous reaction.

On section of a gland in the early stage of tuberculous infection we find it redder than usual, though at times gray and somewhat translucent. The tuberculous granules may be perceived by a glass. They are formed from the vascular and lymphatic vessels found in the cortical and medullary portions, and resemble ordinary follicles, but contain many small cells. Caseation rapidly occurs in them, beginning at the center of the cells, where giant-cells are first formed, proceeding to coagulation necrosis and caseation. A number of these granulations united form the small, yellowish masses, which may be seen by the unaided eye. Caseation is due to vascular obliteration.

The small, yellowish masses, softened at their centers, are surrounded by fibrous tissue due to sclerosis of the stroma of the gland. When this tissue gives way, several masses form a large collection of yellowish, softened material resembling putty. Calcification may occur when the process is very slow.

The specific lymphadenitis blocks the lymph-spaces and thus, for a time at least, mechanically prevents the bacilli from penetrating into the general circulation. Glands not in the stream become infected, this probably being due to the transportation by migrating cells of the motionless bacillus. However, infection usually takes place in the direction of the lymph-current. As the lymph-spaces are obstructed by inflammation products, and entrance of fresh bacilli into the gland is thus prevented, it is the multiplication of those already entered into the gland which gives rise to the tuberculosis. When caseation occurs, nearly all the bacilli have disappeared, but the spores remain, and are capable of reproducing the disease. Suppuration is due to a secondary infection by pyogenic micro-organisms.

The virus of tubercular adenitis is less potent, for the caseous material of a lymph-gland kills guinea-pigs, while rabbits escape, the latter being less susceptible to tuberculous infection.

Taken as a whole, tuberculous adenitis (*a*) is a local disease which may frequently undergo (*b*) spontaneous resolution, but which (*c*) frequently tends to suppuration, the pus being nearly always sterile. It is, however, a constant danger to the system.

Chronic adenitis may, in some cases, be due to continued irritation; ulcers; chronic lesions of the skin or mucous membrane of the bones; periosteum; articulations; chronic inflammation of the viscera, and certain new growths where the adenitis is purely irritative and not yet specific.

PROGNOSIS.—A chronic adenitis may end in resolution, suppuration—caseation (see PATHOLOGY), cretaceous formation, or cyst formation. If all the tuberculous matter can be eliminated, either by nature or art, a recovery may be obtained. The deeper glands are more dangerous than the superficial, as they are extirpated with more difficulty. The great danger of local tuberculous adenitis is that it may give rise to other tuberculous lesions, either *local* (pulmonary phthisis, tuberculous osteitis, white swellings, or abscesses) or *general* (generalized tuberculosis, with rapid death).

Acute miliary tuberculosis may be caused in two ways: either by conveyance through the lymphatic system until the venous system is reached or by the perforation of a vein and the entrance of tuberculous material (Weigert).

TREATMENT.—The general treatment should, in all cases of adenitis, receive considerable attention. **Good food, country air,** and **sea bathing** are of the greatest value.

In peribronchial adenitis the same general methods are to be resorted to. When due to tuberculosis and kindred diatheses and uncomplicated by fever or involvement of lung-tissue, the seashore or the country is indicated. At the seaside children should not bathe in the sea, and should be as quiet as is consistent with life in the open air. **Brisk frictions, milk, a nutritious diet,** and **iodotannic syrup** (2 to 4 teaspoonfuls per day) are effectual measures. After three to four weeks, **emulsion of calcium lactophosphate** and **codliver oil** should be given. **Counterirritation** between the shoulder-blades favors the curative action of the other remedies (Marfan). Applications of **tincture of iodine** between the shoulders, or in some cases **blisters** or, even better, **ignipuncture,** will fulfill the latter indications. The syrup of the **iodide of iron, tincture of iodine, potassium iodide,** or large doses of **codliver oil,** already mentioned, either alone or with **cinchona wine, arsenic,** or **arseniate of sodium,** are the standard remedies usually recommended in these conditions. Not much is to be expected from them, however, unless **outdoor life** is insisted upon.

Extirpation is indicated when internal medication has failed; when glands involve the face and produce deformity; when they are isolated and few in numbers; when they have undergone fibrous degeneration; when they are not freely suppurating. It is contraindicated when there is impaired general health and tubercular deposits in the lungs and joints; when ramifications of the chain of glands are very extensive.

The possibility of giving rise to a

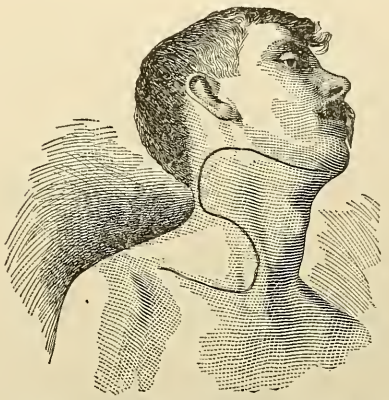
tuberculous process elsewhere by facilitating absorption through exposed tissues should be borne in mind.

One thousand cases of **extirpation** of tuberculous glands, without a single case of pyemia or septicemia and with only 2 cases of erysipelas, in both of which the infection was traced to a nurse. One of the best criterions of the success is the ever-increasing number of patients who present themselves for operation, and who nearly all enter the hospital asking for the removal of their enlarged glands. Milton (St. Thomas's Hospital Reports, vol. viii). Out of 335 children treated, the tuberculous glands were removed in 102. The operated cases gave a percentage of 83.34 cured, and the non-operated 68.77 per cent., that is, 14.56 per cent. in favor of the operation. Generalization of the disease could be found only in 1 per cent. of the cases. Cazin (Lyon Méd., Jan. 11, 1890).

Five hundred and six cases: 286 operated; 220 medically treated. Of the operated cases 149 were carefully followed during three years; 93 (62.4 per cent.) have not shown the least sign of return of the affection. In the remaining 56 cases there was a return. Of the 149 non-operated cases, 28 died in sixteen years (18 per cent.) from general tuberculosis, and 14 are still alive, but have developed pulmonary tuberculosis. Von Noorden (Schmidt's Jährbücher, July, 1890).

In the cases of tubercular adenitis which are not yet suppurating, **extirpation** through a small incision is indicated at once, with medical after-treatment to prevent recurrence. When one hard, caseous nodule exists, it should at once be extirpated, unless the resulting scar will cause marked deformity. When these are multiple, immediate extirpation is the treatment to be followed. Should the adenitis become purulent, extirpation is only indicated after all other methods of treatment have failed. **Local injections** are advised, with a long sojourn at the **seashore,** especially should fistulæ occur. Clean dressings must be applied to the fistulæ to prevent secondary infection. When extirpation is done, it should be complete. A. Broca (Jour. des Praticiens, Oct. 26, 1901).

Senn states that early **operative interference** is as necessary in the treatment of tubercular adenitis as in the treatment of malignant tumors, and holds out more encouragement, so far as a permanent cure is concerned. Tillmann argues that glandular tuberculosis should be operated as soon as possible, in order to prevent general



Sigmoid incision for the removal of cervical glands. (*Senn.*)

miliary tuberculosis by the passage of the bacilli into the system.

After **incision, thorough curetting followed by iodoformization and closure** should be performed. The wound should be **drained.** The operator should not only feel, but see, every gland he removes. In cervical adenitis an S-shaped incision gives more room and a better cicatrix.

In other regions the incision should be made so as to bring its axis parallel with the cutaneous folds. Local recurrence should be treated in the same way. Three or four operations in as many years have been performed by Senn on the same patient, with final successful result.

Mitchell, of Johns Hopkins Hospital, uses a T-shaped incision when making a radical operation for removing all the glands and surrounding fat. The long arm of this incision is made to curve forward over the sternomastoid muscle and starting from the mastoid process joins the short arm along the clavicle, the dissection being carried from below upward and outward from the mesial line, the external jugular vein being tied with two ligatures and divided between them. The omohyoid muscle is then divided, and by using it as a retractor the internal jugular vein is exposed and the sternomastoid muscles pulled aside. In dissecting out the mass of glands the greatest difficulty is experienced with the chain connecting the anterior and posterior triangles behind the sternomastoid muscle, as the spinal accessory nerve passes through the mass and is generally very adherent. It is only when there is very extensive mischief that it becomes necessary to divide the sternomastoid muscle or spinal accessory nerve, or even to tie and divide the internal jugular vein, and these steps should only be resorted to when the advantages of free exposure outweigh other considerations. The wound is closed with a subcutaneous silver suture and drained at its most dependent part. The resulting scar is usually slight.

When many glands are involved and suppuration has occurred, or when periadenitis is present, excision is not to be recommended, as extensive connective-tissue infiltration renders it impossible to remove all the infected tissue.

Subcutaneous extirpation may be resorted to, but the method allows of but imperfect evacuation of the glandular contents and can hardly be recommended.

Drainage of the abscess is a measure which may be recommended for many reasons. A small incision is sufficient for all purposes, and there is practically no scar left.

Mesenteric tuberculous glands should be removed if possible. They are usually discernible as persistent movable tumors beneath the abdominal wall, with anorexia, loss of weight and strength, occasional fever, colicky pains, and possibly mucus in the stools with a tendency to diarrhea.

> Case in a female, aged 25 years, clerk, who had been complaining for one and one-half years of malaise, slight acceleration of pulse, and rise of temperature. She had a movable tumor the size of a hen's egg, one and one-half inches below the umbilicus, in the middle line. The mass was removed. Intestine was resected. No drainage. Patient made a complete recovery. Collins (Interstate Med. Jour., vol. xi, p. 366, 1904).
>
> Case of a man, aged 41 years, who had been ill for six months. He complained of urethral pain before, and pain in the groins after, urination. The tip of the sacrum was so sensitive that he could not sit. Careful examination was negative. Several months later an X-ray picture showed a shadow opposite the third lumbar vertebra, which might suggest renal calculus. Exploratory laparotomy revealed a thin, atrophic appendix, and in the mesentery opposite the third lumbar vertebra was found a caseous and cretified gland the size of a large walnut. Appendix was removed. The gland was **incised, curetted,** and **obliterated with sutures.** No drainage and no gut was resected. Patient made a good recovery. He had no family or other history of tuberculosis. E. M. Corner (Lancet, Dec. 23, 1905).

Less radical measures sometimes bring about a cure. A transformation of the tuberculous tissues into a sclerotic mass may be obtained. A solution

of **chloride of zinc** injected about the tuberculous foci excites a growth of new fibrous tissue, which encapsulates the diseased portion.

Solutions of **iodoform** and **ether** (iodoform, 1 part; ether, 5 parts; distilled water, 5 parts. Injection not to be repeated while iodoform is being excreted in the urine), after Verneuil, in cases where operative procedures are indicated, give a lasting cure, without a cicatrix. These injections seem to exert a beneficial action not only on the tuberculous glands treated, but also on those at a distance from the seat of the injection. Robin uses an injection, **iodoform,** 1 part; **ether,** 10 parts; **oil of sweet almonds,** 100 parts; **creosote,** 2 parts.

The connection between inflammatory conditions of the nasopharyngeal space and acute infections of the glands at the angle of the jaw should be borne in mind. If promptly after the lighting up of the primary inflammation of the gland as evidenced by its enlargement, further absorption of infectious matter from the nasopharynx can be prevented, the gland will cope successfully with the initial invasion and resolution occur, but if fresh invasions are allowed to take place resistance will be overcome and the gland will break down. Attention should therefore at once be directed to the problem of limiting septic absorption from the nasopharynx by measures which keep the mucous membrane clean and also restore it as soon as possible to a normal condition.

Chlorate of potash has an almost specific action in limiting the pharyngeal inflammations of childhood, therefore:—

℞ *Potassii chloratis* ..... gr. j-ij.

Sig.: Every two hours for twenty-four hours, then every three hours, and later every four hours.

To cleanse and soothe the nasopharynx some mild alkaline wash is necessary. Of value in this connection are:—

℞ *Tablets alkaline antiseptic* (*Seiler*).

Sig.: Dissolve one in a half-glassful of water and pour a little with a teaspoon into each nostril every three hours.

The results obtained from this line of treatment were immediately most gratifying. T. S. Southworth (Jour. Amer. Med. Assoc., May 30, 1903).

The following plan is recommended: A salve composed of equal parts of **ichthyol** and official ointments of **iodine, mercury,** and **belladonna,** to be well rubbed in daily, and the bubo covered with gauze dressing, upon which the same salve has been spread thickly. It should be held tightly against the area by spica bandage. If the swelling then breaks down, infiltrate the softest and most prominent part of the swelling with 1 per cent. **cocaine; incise,** empty out the pus from the cavity by pressure, wash out two or three times with **hydrogen peroxide,** diluted one-half with sterile water, then flush with sterile water alone, using an ordinary glass syringe. Melt some 10 per cent. **iodoform ointment** and inject into cavity with some force, to fill it completely. Cover with cold bichloride gauze compress, retained by spica. After five days remove dressing and squeeze out excess of ointment, or reinject if any pus remains. Royster (Medical Record, Feb. 25, 1911).

Camphor-naphthol has proved valuable in some cases. It is prepared as follows:—

℞ *Betanaphthol,*
Camphor .....āā 10 parts.
Alcohol (60 per cent.) ..... 40 parts.

A few drops are to be injected, with antiseptic precautions, here and there throughout the mass of indurated glands, as suggested by Courtin, of Bordeaux.

It is claimed in favor of camphor-naphthol that there is no danger of intoxication and that the treatment is almost painless. Ménard and Calot,

however, have reported cases of intoxication following injection of camphor-naphthol into abscess cavities. The patient suffered from frequent, rapid pulse, loss of consciousness, and epileptiform attacks. The quantity of the drug injected was about 6 drams. This patient recovered. In another case, 8 years of age, 1½ ounces of the solution were injected. In the third case, aged 12, 5 drams. In the last 2 cases life was saved by freely opening the cavity and washing it out on the first appearance of toxic symptoms.

Camphorated guaiacol injected, 4 minims into the center of each gland, causes a rapid diminution of size, and ultimate atrophy. Glands which are beginning to soften should not be treated after this manner. Absolute success obtained in forty-six glands. Simon (Jour. de méd., No. 50, 1904).

Interstitial injections of **iodine,** frequently recommended, usually fail or cause suppuration, owing to the fact that the tincture of iodine is employed. **Metallic iodine,** however, gives good results; the abscess is filled with the crystalline iodine, 8 or 10 applications usually insuring a cure.

Barjou, of Lyons, commends the use of the **X-ray** in the treatment of tubercular adenitis. The principal effect of this treatment is upon the general infiltration which so often accompanies scrofula, uniting the lymph-glands in a solid mass. The glands become separated soon after beginning the applications, and later disappear. If there is any tendency to softening, the rays hasten this, so that the abscess may be opened earlier. The rays continue to have a good effect upon the suppurating tissues. Untoward effects or tendency to cause metastasis are rarely noted.

The **Roentgen-ray** treatment is the most effective method for the treatment of tuberculous adenitis in all its varieties. It affords also the best cosmetic, as well as permanent, results. If treated early the scars are completely avoided—an important consideration, especially in young women, who are often subject to the disease. The treatment is harmless and painless, but must be adapted to the individual. If too weak there will be no progress, and if pushed too far it may be hurtful. It seems also to raise the opsonic index and to produce autogenous vaccines or antibodies, which pass through the patient's system and effect tuberculous lesions at a distance and produce an immunity. The treatment is not confined to the earlier stages, though it is in these that the best cosmetic results are obtained. C. L. Leonard (Jour. Amer. Med. Assoc., May 14, 1910).

Koch's tuberculin and the simultaneous use of the **Bier method** have been used with success in tuberculous adenitis.

After treatment of tuberculous adenitis and other non-pulmonary tuberculous lesions by the injection of Koch's old **tuberculin,** the glands were reduced in size, discharging sinuses healed, and there was neither spread nor recurrence of the disease. The writer reports 10 cases of adenitis, 4 of tuberculous otitis media, 3 of deposits in the pharynx, 4 of tuberculosis of the bladder, 3 of joint tuberculosis, and 1 of tuberculous testicle. In the joint cases **Bier's hyperemia** was added to the tuberculin treatment. Tuberculin stimulates the production of tuberculo-opsonins, and causes a hyperemia around the tuberculous area, thus aiding in the process of inoculation. G. R. Pogue (Med. Rec., Aug. 29, 1908).

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Philadelphia.

ADENOID VEGETATIONS.—DEFINITION.—A definition of *adenoid vegetations,* or *adenoids,* must be somewhat elastic. The name *tonsil* is often applied, and we hear pharyngeal tonsil, third tonsil, Luschka's tonsil, or bursa, used indiscriminately. It would be well to restrict the term *tonsil* to the lymphoid aggregation between the pillars of the fauces, where it was first employed. The word *adenoid* seems to have been proposed nearly two thousand years ago (Wright, "The Nose and Throat in the History of Medicine"), is therefore sanctified by time and usage, and will doubtless be permanently retained.

Lymphoid tissue is a normal constituent of mucous membranes, but the question: When does it become pathological? is not easy to answer. On the one hand we are told that it is abnormal "when visible to the naked eye," and on the other "when it causes subjective symptoms." Many insignificant hyperplasiæ cause a good deal of disturbance, and on the contrary in a stolid, phlegmatic child or in a pharynx of large dimensions very considerable hypertrophies often seem to interfere but little with comfort or health. An accurate definition is desirable, but in view of the fact that lymphoid tissue is a recognized avenue for invasion of the system by pathogenic germs it is most important to determine in what condition of this tissue, healthy or diseased, the process of invasion is favored. Clinically it is clear that, when diseased, it is no longer capable of performing its physiological function and is a detriment to health quite apart from effects due merely to mechanical obstruction. The general symptoms present can hardly be explained on the latter ground alone. A species of toxemia must be also concerned. Distended crypts provide an excellent bed for the cultivation of germs, which find ready access to the circulation in the absence of effecti resistance. Lymphoid tissue may be a portal of entry without itself showing marked pathological change, while it is probable that a dense fibrous adenoid, as met with in older subjects, may offer a firm barrier to bacterial assaults.

SYMPTOMS AND DIAGNOSIS.—It is not safe to rely upon the so-called "adenoid facies" as a diagnostic sign. A very similar appearance is sometimes seen in a subject of intranasal obstruction, while the postnasal space is quite free. A typical case of adenoid hypertrophy in the vault of the pharynx usually wears a dull, listless expression. The nostrils are narrow and pinched; the bridge of the nose by contrast seems widened. The upper lip is retracted, exposing the teeth of the upper jaw, which project and overlap those of the lower. The upper jaw is compressed laterally, so that the roof of the mouth is converted into a Gothic or V-shaped arch. Deflection of the nasal septum may be a result. The nasolabial folds are effaced, and the transverse vein at the root of the nose is unusually conspicuous (Scanes Spicer). The child has a pasty, sallow complexion, and the cervical glands are prominent. The nutrition of a nursing infant suffers in consequence of frequent interruptions due to need of getting air through the mouth. For a similar reason older children "bolt" their food, which being defectively insalivated causes gastric derangement. The latter is further aggravated by catarrhal secretion, always in excess in these cases, finding its way into the stomach. Loss of appetite and

malassimilation are natural sequels. In severe cases deformity of the chest, pigeon-breast (Dupuytren), results from the bad constitutional state, the labored breathing, or from both combined. The mental dullness shown by these children is referred to interference with the lymphatic drainage of the brain and to impaired hearing.

Investigations in 1573 German school children. Of this number 315, or about 18 per cent., were found to have a sufficient degree of impairment of hearing to make a professional examination advisable, although in the majority of them the impairment had not been noticed, either by the patients themselves or by the teachers. In 153 cases the impairment of hearing was directly referable to the presence of adenoids, and in 12 additional cases it was referable to the consecutive changes induced by adenoids which had spontaneously resolved. The number of cases in which adenoid vegetations could be regarded as the causative factor in the impairment of hearing in all the cases considered amounted therefore to about 52 per cent., and the author lays stress upon the importance of a preliminary examination of all school children, both objectively and by hearing tests, at their entrance upon school life, as well as at later stated intervals, and gives the Bezold estimate of 2 meters, for the whispered voice, as the lowest acceptable standard. Cohn (Zeit. f. Ohrenheilkunde, Bd. lii, S. 246, 1906).

An investigation of the occurrence of adenoids in three London elementary schools, with an attendance of 2315, showed that, on the average, about 37 per cent. of the children in elementary schools have adenoids, and that between 72 and 76 per cent. of these have enlarged tonsils as well. On the average, 31.2 per cent. of adenoid cases are mouth-breathers, complete or partial, and hypertrophy of the faucial tonsils may give rise to mouth-breathing in the absence of adenoids. Sex appears to have no influence upon the incidence of adenoids. Adenoids are more common about the age of 8 years, and are next most frequent at about 12 years. True aprosexia is often confused with apparent dullness, due to defective hearing, and it occurs in only about 4.7 per cent. of adenoid cases, is more frequent in girls, and, when present, is associated with a marked degree of adenoids. Macleod Yearsley (Brit. Jour. Child. Dis., Feb., Mar., 1910).

During the last year there have appeared at the Eye and Ear Infirmary in Newark 471 cases of adenoids, all but 166 of which were associated with operations on the tonsils. The writer draws the following conclusions: 1. The condition of inattention and lack of power of concentration is frequently seen in juvenile mouth-breathers, and they are uniformly helped by operation. The effect is immediate and striking. 2. In those young children having the lymphatic tendency and bearing stigmata of degeneracy, the enucleation of the tonsils and the removal of adenoids are followed by most brilliant results. 3. The conditions called choreal, due, as they frequently are, to peripheral irritation, are not only greatly helped, but frequently permanently cured by the removal of the peripheral irritation. 4. In the congenital defects of mental development the mental deficiency is bettered by the removal of the handicap to the general development. 5. He has seen a typical case of mental deficiency of the Mongolian type which showed a marked improvement following the operation for the removal of adenoids. W. P. Eagleton (Medical Record, July 30, 1910).

The term *aprosexia* has been given to lack of ability to concentrate (Guye). Mouth-breathing is a source of much discomfort and even danger. The membranes of the whole respiratory tract suffer from inhalation of improperly prepared air.

Two facts are beyond dispute: The peculiar susceptibility in childhood to

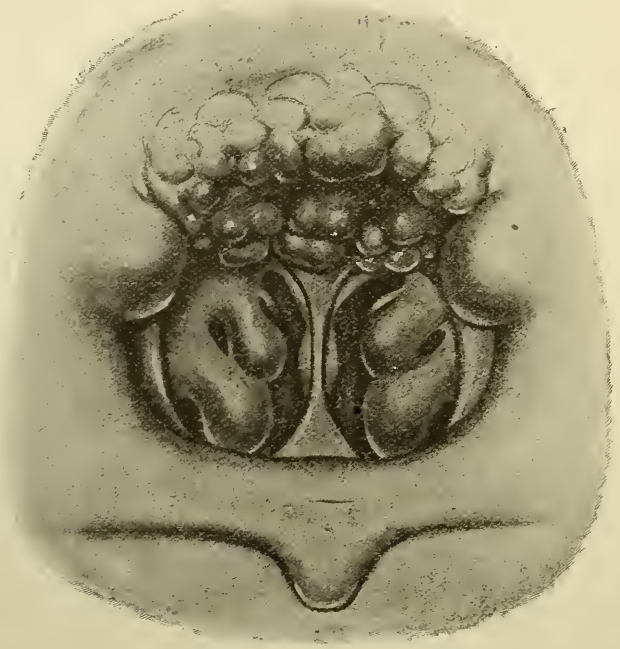
infectious diseases, and the mode of invasion is by the upper respiratory tract. As corollary to these, the following conclusions are submitted: The pharyngeal tonsil possesses a distinct function or functions. This function is of the nature of a defense against the entrance of bacteria, and consists in a certain irrigation of the tonsil surface by a lymph-stream loaded with lymphocytes. This protection function carries with it the inherent qualities of the tonsil to enlarge on the slightest irritation for the affording of further power of defense. This inherent tendency of the tonsil to enlarge is further seen in the frequent recurrence of the tonsil after removal. Strictly speaking, then, in the great majority of cases such enlargements are not a pathological, but a physiological, process. Harris (American Medicine, Jan. 2, p. 20, 1904).

Snuffling and noisy breathing by day and snoring at night are often distressing. Sleep is much disturbed thereby as well as by bad dreams, "night terrors" (*pavor nocturnus*) resulting from deranged cerebral circulation. The effect upon the voice is characteristic. Its non-resonant, "dead" quality always suggests adenoids, at least in young subjects. The ability to precisely locate an obstruction from the sound of the voice, claimed by some, seems to be hardly warranted. In addition to special difficulty with the nasal consonants speech in general is thick and unpleasing. Actual stammering and stuttering have been ascribed to adenoids, and a long list of reflex neuroses affecting the eyes, the ears, and more remote organs has been compiled. Among them may be mentioned laryngeal spasm, hiccough, asthma, hernia, prolapse of the rectum, nocturnal enuresis, chorea, and epilepsy, some of which no doubt have their origin in the imagination of the observer. The relation of laryngeal neoplasms to adenoids is a question of much interest. Even if we decline to accept a theory of "verrucous diathesis," or special predisposition to neoplastic development, it is reasonable to assume that habitual mouth-breathing must irritate the laryngeal mucosa. It has also been suggested that secretions find their way from above into the vestibule of the larynx, and, again, that the extraordinary labor imposed upon the larynx during phonation under these circumstances favors the formation of new growths. In spite of what might be expected, some excellent observers maintain that neoplasms of the larynx are not especially common in adenoid cases. Frequent attacks of earache, of nosebleed, and a tendency to catch cold, are generally included in the list of symptoms. Headache and asthenopia are complained of, the senses of smell and of taste are impaired, and frequently an ichorous discharge excoriates the nostrils and upper lip.

The eyes are often found to be affected in cases of adenoids, the diseases of the eye usually found being: 1. Phlyctenular conjunctivitis (by far the most common). 2. So-called weak ulcer of the cornea, the non-inflammatory ulcer which looks as if a small piece of the corneal surface had been gouged out; sometimes difficult to see unless fuchsin is used. 3. Eczematous keratitis, often called phlyctenular keratoconjunctivitis. 4. A peculiar irritability or hypersensitiveness of the retina, leading to difficulty in opening the eyes in a bright light. There can be no reasonable doubt that these ophthalmic conditions are secondary to the nasopharyngeal: (*a*) By the marked lowering of the general health produced. (*b*) By the actual extension of the inflammatory process up the nasal duct to the eye. Hern (Brit. Med. Jour., Aug. 26, p. 437, 1905).

The writer agrees with Bamberger, Moebius, and other authors in believ-

ing that exophthalmos alone, if not due to mechanical causes, is sufficient ground for making the diagnosis of Basedow's disease. He describes two cases of exophthalmos which were completely relieved by removal of adenoid vegetations. The first case was that of a boy of seven years, with well-marked exophthalmos, accompanied by both Graefe's and Stellwag's signs, and



Posterior rhinoscopic view. (After *Grünwald.*)

who further presented the clinical picture typical of adenoids. Ten days after removal of the pharyngeal tonsil the exophthalmos had completely disappeared. Two years later the patient reappeared with a return of all his symptoms, as a recurrence of the adenoids was again accompanied by bilateral exophthalmos. Radical extirpation of the vegetations was followed by permanent cure of the ocular protrusion.

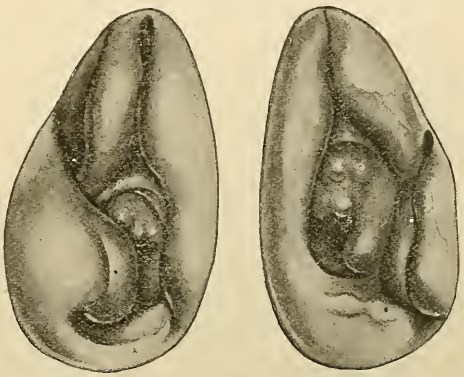
The second patient was also a boy of the same age, who, in addition to adenoids and exophthalmos, suffered from hypertrophy of the tonsils. Amputation of the latter structures was not followed by improvement in the exophthalmos, but a week later the adenoids were removed, and in the course of the next two weeks the exophthalmos disappeared completely. The author is of the opinion that Basedow's disease represents an intoxication of the central nervous system through abnormal internal secretions, and that adenoid vegetations are capable of evoking the malady. Epilepsy and chorea probably have some etiological similarity to Basedow's disease, and the author thinks that they also may be produced by the presence of adenoids. An illustrative case is cited in which clearing of the nasopharyngeal space in a boy of 7 years was followed by the cure of a well-marked chorea minor. It therefore appears advisable to look for adenoids in all cases of these three diseases, and to remove them, even if there is no respiratory obstruction. B. Holz (Berl. klin. Woch., Jan. 23, p. 91, 1905).

In a large number of school children who suffered with blurring vision and fatigue on reading, the author

found nasopharyngeal hypertrophy to be the real cause of the symptoms. Removal of the adenoids and correction of faulty nasal passages resulted in cure in cases where, ordinarily, glasses would be thought necessary. W. M. Killen (Brit. Med. Jour., Sept. 25, 1909).

The picture in the rhinoscopic mirror is unmistakable. Lobulated or fissured masses of various sizes are seen hanging from the vault of the pharynx, obscuring the arches of the choanæ, and often filling the fossæ of Rosenmüller and covering the orifices of the Eustachian tubes. They have been likened in appearance to a "cock's comb" (Czermak, 1860), and they are spoken of by Voltolini (1865) as "stalactite-like growths," a term adopted by Morell Mackenzie. They are often visible by anterior rhinoscopy when the intranasal structures have been shrunken by atrophy or retracted by cocaine. Sometimes the vegetations are distributed down the posterior wall of the pharynx, below the plane of the velum, or they may push forward into the nasal chambers. The view may be masked by viscid or inspissated secretion, and, being foreshortened in the mirror, does not give an adequate idea of the volume of the growth. In some cases, generally in older subjects, the mass is more uniform and cushion-like in appearance, or is bilobed, being divided by an anteroposterior median furrow (*recessus pharyngeus medius*), and is less vascular looking. In adults remnants of adenoids are often seen in the form of bands between the Eustachian cushion and the pharyngeal wall, which doubtless bear some relation to various subjective aural disturbances.

Applications of cocaine and the use of a palate retractor are to be recommended only in older children and when a rhinoscopic examination is imperative. By the exercise of tact and patience it is often possible to get a view, even in a very unpromising case. In some it is out of the question and the only resource is a digital examination. The process is disagreeable to the patient and dangerous for the examiner in children, unless one's finger is protected in some way. A finger shield of metal or rubber may be used, or a mouth-gag may be applied. Better



Adenoids seen through anterior nares. (After *Grünwald.*)

still, the child being firmly held by an assistant, the examiner standing on the left presses the right cheek of the patient between the separated jaws with his right middle finger while he quickly passes his left forefinger into the open mouth and up behind the velum. The mouth cannot be closed and thus the finger is safe.

The anatomical landmarks to be sought are the posterior margin of the vomer in the middle line and the Eustachian eminences at the sides. A novice might mistake a prominent Eustachian cushion, a papillated posterior end of an inferior turbinate, or even the contracted velum (F. H. Hooper) for an adenoid mass, but the

last is higher in the fornix of the pharynx and more posterior and has a distinctly lobulated, elastic, and pulpy feeling, compared to that of a bunch of earthworms. On withdrawal the finger is smeared with blood, which is not the case when a healthy pharynx is explored, unless excessive force has been exercised. In those who object to the finger some idea of the extent and consistence of a postnasal growth may be gained by palpation with a stiff probe or the edge of a rhinoscopic mirror. In some cases a very beautiful view of the vault of the pharynx is given by the ingenious electric pharyngoscope devised by Hays. The end of the instrument having been passed into the oropharynx the patient is instructed to close the lips and breathe quietly through the nose. The palatal muscles relax and permit the light to flood the cavity of the rhinopharynx. With a little patience and care a complete picture may be obtained, even in very sensitive throats. Nasal polypi, retropharyngeal abscesses, syphiloma, and neoplasms, benign or malignant, may occur in this region, but usually present features or give a history which serve to distinguish them.

Benign nasopharyngeal polypi, studied in 22 cases. They are usually unilateral and solitary, and have a peculiar pear-shaped form, the broad end lying in the nasopharynx, while the stalk extends into the nose. They may attain considerable size, and are subject to inflammatory changes which may end in partial or total gangrene. The treatment is very favorable, as they are easily laid hold of, and readily torn out on account of their slender stalk. In the majority of cases the polypi do not recur.

There is usually a profuse discharge of serous fluid after the extraction, and examination of the antrum shows a slight chronic inflammation.

Choanal polypi originate within the antrum of Highmore, and are due to inflammation of the antral mucous membrane. Killian (Lancet, July 14, p. 81, 1906).

It is hard to believe that a simple pendulous polypus of the nasopharynx could be mistaken for a bunch of adenoids. Yet the risk is evidently present in the minds of some observers. In a recent paper by W. A. Wells (Laryngoscope, July, 1911) the fact is noted that it is usually taken for granted that postnasal obstruction in a child under 15 years is due to adenoids. He describes 3 cases of fibrous polypus, which he makes the basis of a plea for intranasal removal with the cold-wire snare rather than by a "mutilating" external operation generally employed in growths of this kind. He enumerates three theories of etiology: (1) cranial, propounded by Nélaton; (2) choanal, that is, springing from the ethmoid, sphenoid, or vomeral region, and (3) sinusal, as adopted by Killian in the paper above quoted. While it is well to bear them in mind, fibrous polypi of the pharynx are so rare and their symptoms are so different from those of adenoids, except in the single feature of obstruction, that the chance of confusion is rather remote.

Rugæ or folds of thickened mucous membrane in the floor of the nose, and the so-called "lateral bands" of red and thickened membrane on the walls of the pharynx behind the posterior pillars (*pharyngitis lateralis hypertropica*) are regarded by some as pathognomonic, but each is often found without adenoids. Fluid injected into one nostril is expected to escape by the other if the nasopharynx is free; by the mouth if adenoids are present (Semon, quoted by Schech). A similar test with oil spray is regarded as "almost abso-

lutely diagnostic" (Bosworth). Each of these experiments must be invalidated by a unilateral nasal stenosis and should not be relied upon.

Adenoids may exist without enlarged faucial tonsils: the reverse is seldom true. Hence it is important to examine the pharyngeal vault in all who manifest the latter condition. The occurrence of adenoids, as well as of turbinate hypertrophy, in victims of cleft palate has often been remarked, whether as an effort of nature to stop the gap or as a consequence of the same diathesis that caused the palatal deformity is hard to decide. Such cases afford unusual opportunity for study of these anomalies.

ETIOLOGY.—A constitutional state allied to struma, termed *lymphatism* (Potain), predisposes to lymphoid hyperplasia. From observation of 1995 cases Sendziak concludes that "scrofula" plays an important part in etiology, a view shared by Lennox Browne. The exanthemata, syphilis, tuberculosis, are similarly accused. Poor sanitation, bad hygiene, and improper diet are undoubted factors, yet not infrequently cases occur in which none of the foregoing elements is concerned and we are at a loss to discover the cause of the condition.

The importance of nasal stenosis, resulting perhaps from some injury in early life, is generally admitted. Behind an obstruction the air is so rarefied on inspiration that congestion of the mucous membrane results with consequent tendency to hyperplasia. The bearing of this fact with reference to treatment should be appreciated. The habitual breathing of impure air, or of air too hot or dry, often prevailing in our homes and sleeping rooms, no doubt has a bad effect on the mucous membranes. The same is true of certain occupations that involve the inhalation of irritating vapors or floating matter in the air. The condition occurs with equal frequency in the two sexes. It seems reasonable to admit an inherited proclivity. Those who deny the existence of heredity find it difficult to explain the exhibition of almost identical local conditions in several successive generations. The effect of a rigorous climate is not necessarily bad, but extremes and sudden changes of temperature and humidity are no doubt harmful.

Adenoid growths are essentially a disease of early life, of the formative period, when the lymphoid tissues are especially active. A few congenital cases are on record. Among 437 children in the first three years of life examined by W. F. Chappell not a single example of lymphoid hypertrophy under the age of three months was found.

> Some instances of adenoid vegetations in infancy appear to be truly congenital, symptoms referable to the condition being present at birth. A considerable number of infants suffer from slight degree of adenoid vegetations, as evidenced by mild symptoms of nasal obstruction and catarrh. But there are also not a few cases in which more severe and even grave symptoms may be present. These will materially interfere with the health of the infant, and do not tend to improve with ordinary medical treatment. There are several forms of the affection: the first, in which there are marked nasal obstruction and catarrh, with or without epistaxis; the second, in which reflex phenomena are the principal manifestations of the trouble, without any real nasal obstruction (such signs may be convulsions, laryngeal stridor, and vomiting); the third, those in which secondary septic affections predominate, these being chiefly

septic adenitis and otitis media, and, lastly, those cases in which nasal obstruction is present and is associated with nervous and septic conditions. In by far the larger number of cases of adenoids in infancy, the symptoms are slight and do not call for active operative treatment, but, on the other hand, there are certainly some cases, comparatively few in number, in which the signs and symptoms are such as to demand removal of the adenoid growth. In these the improvement that follows operation tends to confirm the fact that the various phenomena that the infant presents are, in reality, due to the lesion in the nasopharynx. R. C. Dun (Lancet, August 15, p. 474, 1903).

Adenoid vegetations are present in nursing children more frequently than is usually supposed. The symptoms are difficult and noisy nasal respiration, and there is usually some nasal secretion. In advanced cases there is marked dyspnea, laryngeal spasms, disturbed sleep, and restlessness during waking hours. The nutrition is diminished, the skin pale, and the cries are weak and changed in their timbre. The first development of these cases is hard to establish because it is exceptional that a specialist is consulted, and frequently the little patient succumbs to a progressive inanition; if it survives, it grows with the characteristics of adenoidism.

If, on the other hand, the proper treatment is followed, the transformation is complete; the mechanical difficulty of respiration ceases, the nutrition improves, the child gains rapidly in weight, and recovers its normal quietness and sleep. F. Massei (Revue Hebd. de Laryn., etc., Oct. 22, p. 499, 1904).

Very little consideration is usually given to the presence of adenoids in the infant, although they are common and their evil results even greater than in childhood. The anatomical construction of the pharynx and postnasal space in infants makes a small amount of adenoid tissue a marked impediment to respiration. They are directly responsible for the attacks of otitis media so often seen in infants. J. L. Morse (Jour. Amer. Med. Assoc., Nov. 9, p. 1589, 1907).

The writer criticises the neglect of adenoids in early infancy, as they interfere with the proper development of the child by reflex action, by the irritation they produce and the obstruction they cause. The postnasal pharynx at birth is a space only one-quarter inch high by one-third inch wide, so that a very slight adenoid hypertrophy at this period will cause obstruction. At the end of the first year it is nearly doubled in size. It often produces symptoms in the first days of life, and the mistake is sometimes made of diagnosing specific disease. The snuffles are specially marked while the child is nursing and result from an adenoid which produces irritation, and, if large enough to obstruct the pharynx, there is mouth-breathing. Other causes may produce mouth-breathing, but adenoids do so most frequently during the first year of life. A third indication of the condition is the appearance of recurrent colds, which, during the first year, are usually caused by adenoids. Another most characteristic sign is a persistent cough, sometimes simulating whooping-cough, without any other indication in the pharynx or bronchi to account for it. A fifth and most dangerous condition is otitis media. It is not always easy in a very young infant to determine the presence of adenoids, but it can be done by rapid manipulation. The right index finger being rapidly passed into the mouth while the jaw is held open by the ends of the fingers of the left hand pressing on the teeth, the rough surface of the adenoid can be detected by the skilled physician and sometimes so quickly that the baby does not even cry. R. G. Freeman (Jour. Amer. Med. Assoc., Aug. 21, 1909).

From a study of 32 cases Erdely concludes that adenoids are congenital and should be removed in children after the sixth month if symptoms are present. (Jahrb. der Kinderh., May, 1911.)

Rare instances have been noted in the aged, but the tendency is toward atrophy after puberty. Several cases in elderly people have been observed by Bryson Delavan, who holds the belief that the condition may develop in middle life and is not necessarily a legacy from childhood. One was discovered by J. Solis-Cohen in a woman of 70, and a number of authentic cases after the age of 60 have been reported (P. G. Frank), but at this time of life a malignant element is always to be suspected. The curious observation has been made by Gellé that these structures sometimes show renewed activity at the menopause.

> Series of 57 cases found in literature in which a considerable amount of tissue was found in the pharyngeal vault of adults. In most cases it was possible to make the diagnosis by posterior rhinoscopy, but sometimes it was necessary to use the finger. The growths varied in size and distribution, but were always of considerable size, and usually sprang from the angle between the roof and posterior wall of the pharyngeal vault. They were usually soft, pulpy, and friable, particularly so in the older subjects. Thirty of these cases were between 20 and 30 years of age, 15 between 30 and 40, and 12 over 40 years of age. Thirty-six had throat symptoms, 25 ear symptoms, 10 tuberculosis, 1 cervical adenitis, and 1 ethmoiditis. The sexes were nearly equally divided. The improvement following operation was much better in the decade between 20 and 30 years of age than in patients over 40. D. M. Barstow (N. Y. Med. Jour., May 6, p. 899, 1905).

PATHOLOGY. — Lymphoid cells embedded in a reticulum of connective tissue containing small blood-vessels and nerves, the retiform adenoid tissue of His, and enclosed in a mucous membrane covered by columnar ciliated epithelium, constitute adenoid vegetations. The relative proportion of these elements varies with the age of the patient, the duration of the disease, and the frequency and intensity of acute inflammatory attacks, to which this tissue is very liable. In young subjects cells predominate and the tissue is soft, friable, and vascular; in older ones connective tissue is in excess and the mass is more dense and hard.

As a matter of clinical convenience adenoids are sometimes divided into soft and hard, which are, of course, merely grades of the same pathological process. In very young children, also, a temporary intumescence takes place in consequence of gastrointestinal disturbance or other cause, when many of the subjective symptoms of adenoids are presented. This condition, naturally, calls for different treatment than an organized hyperplasia. Morbid changes are not confined to the epipharynx, but involve adjacent lymphoid structures. Cystic transformation and other disorders of the pharyngeal bursa have been particularly described by Tornwaldt. A cyst of the bursa may reach extreme dimensions and occasionally small cysts are met with in the adenoid tissue, but the importance of these conditions has been somewhat exaggerated. The idea once expressed by Woakes that adenoid vegetations are papillomatous in structure is not sustained by modern views.

PROGNOSIS.—Under present-day methods of attacking the disease the prognosis is good, both as to arrest of the morbid process and relief of associated symptoms. Only in case the condition has been extreme in degree or duration organic changes may have been established, for example in the ears, which are irremediable. Chronic otorrhea due to adenoids cannot be cured

while the latter are allowed to persist. Likewise impaired hearing and tinnitus due to occlusion of the Eustachian tube from pressure or congestion must be reached through removal of an adenoid mass. Recurrence of adenoids may take place in certain cases of pronounced lymphatism (status lymphaticus), in which predisposing factors cannot be wholly eliminated, or when an operation for removal has been done very early in life. The suspicion remains, however, that some alleged relapses are really examples of incomplete removal. These partial operations are explained in a measure by A. A. Bliss on the ground that the lymphoid tissue penetrates the fissures of the vomerosphenoidal articulation (*canales basis vomeri* of Harrison Allen), where it is more or less inaccessible. Extreme vascularity of the region and the fact that the adenoid is often made up of separate and distinct bundles also contribute to the possibility of apparent recurrence, which is really a growth of tissue that has evaded the knife.

It is safe to say that no operation in the upper air tract confers more gratifying and positive benefits than an adenectomy properly done. There has been much controversy as to the thoroughness with which morbid tissue should be removed, one side advocating extirpation of every vestige and the other averring that such a course is ultraradical. When we reflect upon the wide distribution of lymphoid tissue in the so-called ring of Waldeyer, or lymphoid triangle, the conclusion is forced upon us that absolute eradication is impracticable, even if desired. What we accomplish in a given case is extraction of the most salient and diseased portions: the consequent improvement in air supply and in other respects enables nature to do the rest. This statement is not to be taken as a defense of superficial operating, or as a suggestion that we may trust nature to supply defects involved in our own negligence. Postoperative shrinkage of any considerable remnants is not to be expected, yet there are limits of safety beyond which we may not pass and anatomical conditions which are insuperable. Certainly erasion of the mucous membrane through its whole thickness, so as to replace glandular secreting tissue by scar tissue, is to be strongly deprecated.

Case of a child of 7 years, who had been operated upon three years earlier for adenoid vegetations without accident, but without benefit. A second operation was performed two years later, after which, on returning home, the patient passed a great deal of blood by vomit and by stool. A third operation for enlarged tonsils was also performed without special incident. Nevertheless, the child never breathed freely by the nose, and continually kept the mouth open. The writer found an incomplete adhesion between the soft palate and the pharynx consecutive, in all probability, to the second intervention. The pharyngeal orifice behind the uvula was too small to permit the passage of an adenoid curette. On being enlarged the opening offered ample space for respiration. Courtade (Annales des mal. de l'oreille, du lar., du nez, et du pharynx, Aug., 1910).

Case of a young woman suffering from nasal insufficiency, due to the presence of large adenoids, removal of which was followed at once by commencing atresia. The case being referred to the writer, he advised operation, but this was declined. The closure soon became complete, and in May, 1909, she consented to operation. An incision was made through the adhesion, and a strip of gauze was passed through the nose into the mouth, and the ends attached over

the lips. This was left for three days, when sloughing commenced, and, fearing extensive destruction of tissue, the gauze was removed. Subsequent treatment consisted of dilatation twice a day with the probe or finger. When reported, six months later, the pharynx was perfectly free and the patient's voice was normal. Wolff Frudenthal (Laryngoscope, May, 1910).

Adenoid tissue is present in the vault of the pharynx in 1 out of every 4 recruits. The fact of its presence should be noted on the record of the physical examination in order that due weight may be given to it as a factor in producing defective hearing when cases of this sort come up for discharge for disability or pension. All large adenoids should be excised on entry into the service, and smaller masses if associated with pathological changes in the middle ears. Refusal to consent to operation should disqualify applicants for enlistment in the artillery branch of the service or transfer to that branch. Every 2 out of 3 recruits who have adenoids have visible changes in the middle ears. Fifty per cent. of the cases who do not have adenoids, but who do have hypertrophied tonsils, have changes in the middle ears. Changes in the middle ears without the presence of either adenoid or tonsillar hypertrophy are unusual, and occur in only 1 case out of 12, and in the case in which it occurs it is usually associated with hypertrophic rhinitis. In other words, in 11 cases out of 12 which show changes in the middle ears, adenoid or tonsillar hypertrophy will be found. One out of every 3 cases with adenoids will also have hypertrophied tonsils. Two out of every 3 cases with hypertrophied tonsils will also have adenoids. Recruits with marked hypertrophy of the tonsils should have the glands excised, whether they have had repeated attacks of acute tonsillitis or not. Adenoids do not undergo spontaneous atrophy in young adults. Le Wald (Military Surgeon, May, 1910).

In a small proportion of cases breathing by the natural channels is not at once resumed. This is due simply to the *habit* of mouth-breathing, or to imperfect development of the air tract from prolonged disuse. In the former case the habit is soon corrected by some device for binding up the chin and keeping the mouth closed during sleep. In the latter the difficulty is greater and it may be a long time before the normal respiratory current is restored. These cases, fortunately rare, are most disappointing to operator and parents and yield, if at all, only to careful attention to hygiene and to measures tending to promote development. The co-operation of the dentist is enlisted for correction of the oral deformity, widening the dental arch and thus depressing the floor of the nose and increasing the diameters of the nasal passages. It is best not to delay this beyond the sixth or seventh year (E. A. Bogue), although surprising results may be achieved much later.

Two other causes of continued difficulty in breathing after adenectomy have been described: one is extraordinary prominence of the bodies of the cervical vertebræ (J. E. Newcomb), and the other is a paresis of the suspensory apparatus of the hyoid bone and the tongue, so that, when the muscles are relaxed in sleep, the tongue falls back and occludes the glottis (Harrison Allen).

In the experience of Payson Clark mouth-breathing persisted in 35 out of 75 cases whose subsequent history could be learned. Over 500 others were not traced and it is fair to assume that the above percentage might be greatly reduced.

Faulty habits of speech are to be reformed by careful exercises under com-

petent supervision. The palatal muscles having been long curbed in their action need to be properly educated.

TREATMENT. — Until Wilhelm Meyer, in 1868, gave to the world the results of his careful studies, but little had been done in diagnosis or treatment of adenoids. A few scattered references are found in literature many years before his day, and the valuable researches of Luschka and others in the anatomy of this region are well known, but no serious attempts were made to remove from the postnasal region certain obstructions, and their exact nature was not fully understood until Meyer began his investigations.

In the hope of escaping surgery various local astringent applications and methods of treatment have been advised, all of which are more or less futile, except in the vascular or "cyanotic" adenoid of some writers. In these cases instillations of **adrenalin chloride**, 1 to 5000, followed by fine sprays or vapors of **mentholized albolene** are of service. Glycerite of tannin and other astringents can have little or no permanent effect while the underlying cause remains. Anemia, gastrointestinal derangements, or other disorders must be corrected by proper **hygiene, diet,** and **general medication** as indicated.

Internal medication offers but little. With anemic or chlorotic children one is often inclined to temporize and try to build up the system by means of **iron** and other tonics, but the speedy improvement in general condition following surgical intervention is conclusive proof that the main cause of the constitutional depression lies in the local disorder, upon which medication alone has little or no effect.

Experience with **opotherapy** is still too limited to justify a final verdict. Some authorities assert that under its use reduction in volume of lymphoid hypertrophy is so rapid as to eliminate the necessity of surgical intervention. In this connection attention is drawn to the danger of too thorough eradication lest neighboring glands be stimulated to excessive functional activity and increased growth.

The internal and local use of iodine for its sorbefacient effect has not had pronounced success. The Bier suction hyperemia treatment, for which very temperate claims are made in hypertrophy of the faucial tonsils, does not seem to have been applied to adenoids. The tubes figured by Meyer-Schmieden for aspirating the nasal chambers and the sinuses would make but little impression in the postnasal space, although good results in atrophy of the nasopharynx are mentioned.

At one time certain "breathing exercises" were loudly vaunted as a cure for adenoids. The shallow character of respiration practised by most people and the health-giving value of deep breathing are generally comprehended in these days, especially in connection with the class of cases under consideration. Meyer appreciated the fact that a dense hyperplasia cannot be dissipated by breathing exercises, or by measures tending to promote the general health, or designed to exert a contractile effect upon the morbid growth. His early essays at removal were made with a small "ring knife" passed through the anterior naris and guided by a finger inserted behind the velum. It was soon found possible to operate more easily and expeditiously through the mouth, and in consequence today the instrument shops are flooded with forceps,

guillotines, and curettes designed to facilitate this procedure.

In adopting a plan of operation the principles of thoroughness, gentleness, and celerity are to be observed. By the first is meant not a clean sweep of all the soft parts down to the bone, but a removal of projecting tabs that can be detected by the examining finger. The second is insured by selection of instruments that include in their bite generous segments of tissue. Thus the need of frequent reintroductions is obviated and the parts are spared unnecessary violence and contusion. Finally, while undue haste is to be avoided, it is well to abbreviate as much as possible the period of narcosis. We are prone to underestimate the importance of this detail. As a matter of fact, a large proportion of accidents, both immediate and secondary, can be traced to excessive crowding of the anesthetic at the hands of one who is not expert in its management. General anesthesia should always be in charge of one trained for the duty, who knows how to get satisfactory relaxation with a minimum of anesthetic.

Preparation of the Patient.—While adenectomy may not be properly considered a major operation, yet it is by all means to be postponed in the presence of any acute local disturbance, or of concurrent general disorder, or when an epidemic of any contagious disease is prevailing. The advice once given by Lennox Browne to operate during an attack of diphtheria, with a view of averting the necessity of a tracheotomy, is refuted by the modern mode of treatment in that disease. Locally an attempt to secure an aseptic operative field by the use of antiseptics is hopeless. The parts should be cleansed of secretion by douching with warm normal salt solution, but anything beyond that is superfluous. Nasal stenosis from overgrowth or deformity should be corrected at the same time, or by a preliminary operation if very extensive. Large faucial tonsils which interfere with manipulations should first be excised.

Bleeders should be avoided, or prepared by a few doses of calcium chloride or lactate. The strange conflict of opinion, both in the laboratory and in the clinic, as to the effect of calcium upon the coagulability of the blood tends to weaken confidence, but possibly should rather teach us to use it in larger doses than has hitherto been the custom. The weight of evidence is strongly in favor of calcium lactate, some authorities asserting that the chloride is practically inert (W. K. Simpson). The former is more agreeable to take, and thus far no unpleasant consequences from larger doses have been experienced.

> Clinical experience shows that **calcium lactate** has a controlling influence in hastening the coagulation of the blood. Its efficacy is more marked in hemophilic cases where the coagulation is delayed than in cases of normal coagulation time. Before operation, especially on tonsils and adenoids, careful inquiry should be made relative to any hemophilic heredity or tendency. In suspicious cases the coagulation period should be determined before operation. It is questionable, if not positively contraindicated, whether such operations should be undertaken in hemophilic cases other than under the most extreme urgency. In all cases of operation for the removal of tonsils and adenoids, calcium lactate should be given for a period prior to and after the operation, both for its possible effect in diminishing the immediate hemorrhage and in preventing secondary surface hemorrhage.

Of the calcium salts, the lactate is more positive in its results, is more agreeable to administer, and is less irritating to the stomach. Simpson (Medical Record, Sept. 25, 1909).

The bowels should be evacuated by a **saline laxative** and no solid food and no milk given for at least six hours beforehand.

Position of the Patient.—The *erect* position is advocated by some, because it is that to which we are accustomed in routine work, the loss of blood is less, and *débris* and blood tend to escape forward rather than backward toward the glottis. Moreover it is thought that the ears are in less danger as a result of freedom from accumulations at the openings of the Eustachian tubes. The position *on the side* is favored by others on account of the tendency of blood and secretions to gravitate to the dependent side and drain off through the nose and mouth.

After all has been said, the *recumbent position* seems to be the most convenient for all concerned and is free from risk, provided the anesthesia be not profound and the reflexes are preserved. In such case foreign material approaching the larynx is promptly ejected, and what finds its way into the stomach is thrown up before complete recovery from the anesthetic. With attention to this point, the so-called Rose's position, the head being dependent, is not essential. In adults and under local anesthesia the upright position is preferable.

When the operator selects the recumbent position, the body should be horizontally on the back, the head being neither flexed nor extended. With the head extended the cervical curve of the spinal column is increased. In this position the operator is liable to cut deeply into the structures of the posterior pharyngeal wall, which will be stripped down by the curette. A lateral position favors the drainage of blood from the pharynx and in no way inconveniences the surgeon in removing the tonsils. For the latter purpose a small guillotine is better than a large one, and is not so liable to slip. F. C. Carle (Lancet, May 13, p. 1265, 1905).

Anesthesia.—In children under one year the adenoid growth is so soft and friable that it can be readily broken down with the fingernail and no anesthetic is necessary. An artificial nail adjusted to the fingertip (Creswell-Baber, Motais) has no advantage over a curette, and rather hampers freedom of manipulation. Local anesthesia with **cocaine, stovaine,** or **alypin** is reserved for adults and for children old enough to be manageable.

Method of anesthetizing the pharyngeal tonsil by infiltration, the needle being passed through the nostril. First of all, a camel's hair brush is soaked in a 10 to 20 per cent. solution of **cocaine,** passed through one nostril, slightly upward toward the upper border of the posterior nares, and left there for a few minutes. The process is repeated on the other side. The deeper parts are caused to shrink, so that the upper border of the posterior nares and the adenoid tissue behind becomes visible by anterior rhinoscopy. The camel's hair brush is then gently rubbed over these parts until they are superficially completely anesthetic.

To anesthetize the pharyngeal tonsil proper, the most satisfactory drug is B-eucaine in a warm 5 per cent. solution with 0.8 per cent. of NaCl. Cocaine is unsuitable, as more concentrated solutions are required than are necessary for ordinary infiltration anesthesia. Novocaine is unreliable. The **eucaine** solution can be sterilized by boiling, is but slightly toxic, and is not followed, as are the vasoconstrictors, by secondary paresis and hemorrhages. Its action is increased by the addition of 5 drops of **adrenalin** to each syringeful. The capacity of the syringe employed by the writer is

slightly more than 2 c.c. (about 34 minims). The needle is passed into one nostril backward and slightly upward toward the upper margin of the orifice of the posterior naris, where it impinges on the mucous membrane of the anterior part of the roof of the pharynx, and the insertion of the pharyngeal tonsil a short distance external to the septum. This should be done under the guidance of the eye.

Considerable pressure is required to force the fluid into the tissues, and an easy flow indicates that the needle has not traveled sufficiently upward to the pharyngeal roof. The process is repeated through the opposite nostril, half a syringeful being injected on either side. After waiting a short time the adenoids can be removed, in the great majority of cases entirely, painlessly. F. Hutter (Wien. med. Woch., Oct. 10, p. 2263, 1908).

Although certain statistics, like those given by C. A. Parker, from Golden Square and St. Bartholomew's Hospitals, are partial to chloroform, it is the general belief that this agent is especially dangerous in lymphatism and should never be used (F. W. Hinkel). The danger is said to be less when it is joined with oxygen. **Nitrous oxide gas** is universally admitted to carry the least risk, but it is too transient for any but the simplest case. Combined with **oxygen,** its effect is slightly more prolonged and in other respects it is satisfactory (W. E. Casselberry). When used as a preliminary to **ether** in what is known as the *gas-ether sequence,* with a Bennett inhaler, the process of narcosis is rendered as agreeable, rapid, and safe as possible. By this method a much smaller quantity of ether is needed with proportionate reduction in stimulation of mucous secretion and less of unpleasant after-effect, two of the chief objections to ether. Braden Kyle quotes Royer to the effect that secretion is lessened by adding to the ether a few drops of **oil of Hungarian pine.** The disagreeable odor of ether may be partially prevented by first pouring a little cologne water in the mask, and thus the confidence of a timid patient may be secured. By many operators the "drop" method of giving ether is preferred, especially in young children, and thereby the strain upon the chest walls incident to the use of a closed inhaler is avoided. By some the use of **morphine, atropine,** or **chloretone** to reduce mucus secretion is advised. A clear operative field may be procured with the ingenious suction apparatus advocated by Alexander and Gwathmey (N. Y. Med. Jour., March 11, 1911).

Those who oppose general anesthesia refuse to admit the fact that the shock without it, especially in a nervous child, overbalances any risk incurred when the plan just outlined is pursued. It is almost indispensable when, as often happens, the palatal tonsils must be removed or other instrumentation done at the same time.

Ethyl bromide and **ethyl chloride,** the latter said to be the less objectionable, have no supreme advantage and are not proved to be free from risk. According to Lermoyez, the difficulty in regulating the dose of ethyl chloride, owing to its great volatility, is overcome by giving it with a suitable mask, whereby the quantity inhaled is precisely known. The Apperson inhaler is highly recommended, from 3 to 5 grams of the anesthetic being required for a short operation. The drug is so rapidly eliminated that after-effects are few or absent. Other good features claimed for it by

those experienced are ease of administration and rapidity of action. It may be given prior to other anesthetics, or alone continuously for an indefinite time without regard to the position of the patient, upright or prone (G. F. Hawley).

At the Royal Infirmary of Edinburgh, the experience of T. D. Luke has been so gratifying that he recommends ethyl chloride as a matter of routine for short operations. On the other hand Z. Mennell, at St. Thomas's, London, notes the frequent occurrence of pulmonary embolism at that institution since the introduction of ethyl chloride. He attributes it to increased coagulability of the blood caused by the drug, and on this account has abandoned its use. Those who advocate ethyl bromide ascribe disasters with it to the use of an impure product, or to the mistake of having substituted for it ethylene bromide. In addition we are enjoined to give it *en masse,* admitting no air, and to continue the administration no longer than one minute (A. R. Solenberger). Most operators will find sixty seconds too short a time for thorough work.

The **Schleich inhalation mixture** (E. Mayer) and the **A. C. E. mixture** are urged by some, but have no special attraction.

If the operation is to be done in the upright position, it is customary to give the anesthetic to the patient lying down and to slowly elevate the body when all is ready. Special operating chairs have been devised for this purpose (T. R. French).

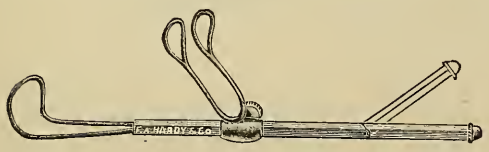
The question of safety being of the first importance, too much stress cannot be laid upon the necessity of choosing a reliable anesthetic and a trustworthy anesthetist.

It would be strange if in this psychotherapeutic era an escape from the annoyance and risks of general anesthesia were not sought in the line of suggestion. Accordingly we find proposed "**mental suggestion** as a substitute for anesthetics in the removal of tonsils and adenoids from children" (F. D. Gulliver). The number of children amenable and of operators capable of exercising the requisite psychic influence must be extremely small. Yet the method is said to be in successful operation in one of our large metropolitan clinics.

Insufflation anesthesia, or the forcing of ether vapor to the lungs through a tracheal tube (Jackson direct laryngoscope), is pronounced by C. A. Elsberg, of Mount Sinai Hospital, who introduced the method and devised an excellent apparatus for the purpose, "ideal" in operations in the upper air tract, as regards prevention of aspiration of blood and mucus and as to rapidity and safety of narcosis. This view is confirmed by C. H. Peck from experience with a number of cases at Roosevelt Hospital. The numerous experiments by S. J. Meltzer at the Rockefeller Institute justify his opinion that it is the "safest and most effective way" of administering ether. He finds **chloroform** far less safe, but it may be given for short operations with confidence under proper supervision. Recovery is said to be prompt and free from the usual discomforts. In using this method the anesthetist avoids interfering with the operator. Another great advantage is that it permits giving a supply of air to the lungs without the action of the respiratory muscles, if, perchance, artificial respiration becomes necessary.

Instruments and Methods.—Chemical caustics and the electric cautery have been generally superseded by instruments for extracting the morbid tissue instead of destroying it and allowing it to slough away.

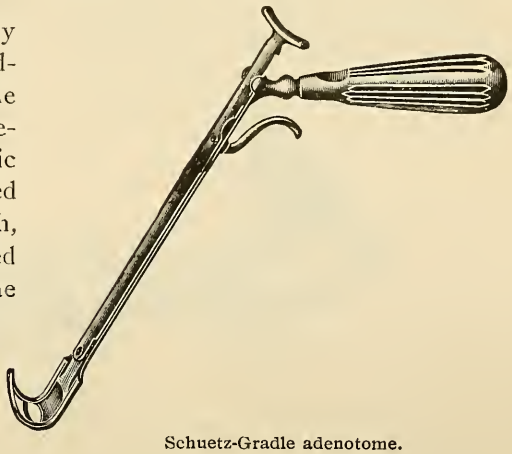
Caustics are available, if ever, only in tractable patients and under guidance of the rhinoscopic mirror, the palate being held forward with a retractor (White) or by means of elastic ligatures (flexible catheters) passed through the nares and out of the mouth, the nasal and buccal ends being tied or clamped together. Under **cocaine** the process is not extremely painful. **Silver nitrate** and **chromic acid** have been used in this way. Without the utmost care and the use of a guarded applicator there is danger of excessive damage and violent reaction. The **electric cautery** point or loop is more precise and manageable, but at best these methods are tedious and unsatisfactory. They are reserved for hematophiliacs and those who refuse to be cut. In other cases the cold-wire snare, the guillotine, forceps, and the curette provide a wide choice of cutting instruments. A straight snare (Jarvis)



White's palate retractor.

may be passed through the naris, or a curved one behind the velum (Bosworth). It is successful only when the lymphoid tissue is so bunched in the vault that the wire can readily encircle its base. It is apt to slip and include only superficial portions.

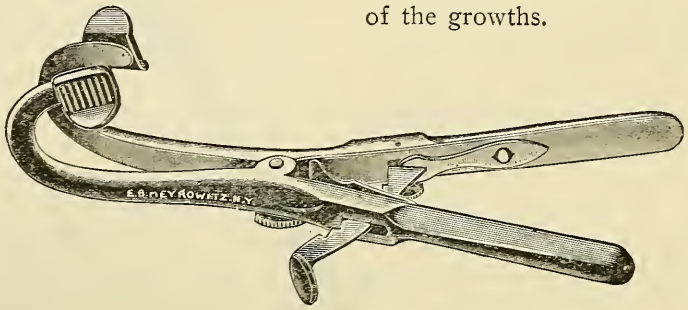
The guillotine or adenotome of Schuetz, modified by Gradle, works admirably in the vault, but not on the lateral walls. We have finally a great variety of forceps and curettes adapted to any age or situation. It is well to have several sizes, large for the main operation and small for the fossæ of Rosenmüller and the choanæ. The majority of forceps cut laterally; those of Schuetz cut anteroposteriorly. The edges not crossing like scissors, the operation is practically a combination of avulsion and cutting. The small forceps of Hooper cross slightly, and the large fenestrated blades of Gradle's forceps have a defined scissors action.



Schuetz-Gradle adenotome.

The writer advocates operating without systemic anesthesia whenever feasible, since he notes that the statistics show a disproportionately large number of deaths when chloroform is used. With proper skill the operation can be done as effectively in the wide-awake child as in the anesthetized subject. Nor in his own practice has he noted any unpleasant sequels of operation. He uses for ordinary adenoid operations no instrument but the guillotine-shaped adenotome of Schuetz of his own modification. This brings out the whole tonsil intact. When the adenoids are extensive the instrument is pressed firmly toward one Rosenmueller fossa,

and after its action is reinserted toward the other side. The work is done quicker, with less hemorrhage, and as efficiently as with any other instrument. He abolishes actual pain almost completely by injections of 20 per cent. **cocaine solution,** supplemented by adrenalin applied to the pharynx up to its roof. Gradle (Chicago Med. Record, Nov., p. 634, 1907).

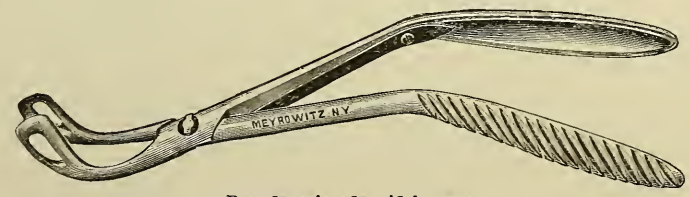


Denhard's mouth gag.

The early instruments for scraping ere the sharp spoons of Justi and of Trautmann. Curettes are now made larger and of different sizes and shapes, and some are provided with forks to catch the resected fragments. Such complicating attachments are a disadvantage rather than otherwise. The simpler the instrument, the easier it is to handle and keep aseptic.

While the anesthetic is being given, the patient lies flat on the back. After the muscles are somewhat relaxed, a Denhard mouth-gag is inserted on the left side. The operator stands on the patient's right. If the palatal tonsils are enlarged, they are first removed with snare (Farlow, Moseley), tonsillotome (Mackenzie, Mathieu), or punch (Myles, Roberts), and the patient is quickly turned on the side to allow blood and secretion to drain. Bleeding having subsided, the patient is replaced on the back. A little more anesthetic may now be required. The nasopharynx is explored with the finger to determine the extent and distribution of the growths.

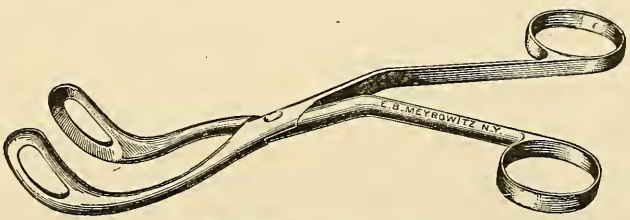
The soft palate being dragged forward with the left forefinger, a forceps with large blades is passed into the vault, opened to full width, and while the left index finger presses the blades firmly upward the instrument is tightly closed. The forceps of Brandegee, or the author's, is preferred. Then by a slight twisting movement the pendulous masses which have been seized are torn from their attachments. Again the patient is turned on the side. After a few moments the pharynx is explored for remnants which need to be removed with small forceps (Gleitsmann, Loewenberg) or curette under guidance of the finger. By many operators a curette



Brandegee's adenoid forceps.

of the Gottstein or Beckmann pattern is used for the whole operation. A curette of proper shape and size, and correctly used, certainly sweeps off the tissue most effectually. The blade, always quite sharp, is slipped behind the velum and crowded from below upward close to the posterior margin of the vomer, and then by a quick movement pushed backward and slightly downward through the base of the growth. The blades are directed by the finger passed behind the velum, and in any case it is a useful instrument for clearing out the postnasal arches, where fragments are sometimes missed and afterward give trouble.

Even when the postnasal adenoids have been completely extirpated, the part is apt to remain vulnerable for some time, often highly sensitive to atmospheric changes, so that the attacks may not altogether cease until steps have been taken to brace up the relaxed mucous membrane and reduce its susceptibility to chills. It is, therefore, advisable to remove the patients, soon after the operation, to the seaside, choosing a situation which is moderately bracing, but not bleak. He should be taught to breathe as much as possible through the nose, and should pass the greater part of his time in the open air. There are two applications which are very serviceable in these cases. Twice a day a solution of **resorcin in normal saline** (5 or 10 grains to the ounce, with the addition of half a dram of tincture of **hamamelis**) should be instilled into the nostrils as the child lies on his back with his head supported by a pillow. Five or six drops may be used to each nostril with a "dropper," allowing the fluid to trickle down into the pharynx. After using these drops for a week we can begin



Knight's adenoid forceps.

A clean complete removal is thus ensured at least as to the vault itself, when the conformation of the region is normal. Unless the blade is passed close to the posterior surface of the velum and is made to hug the vomer in its upward movement, pendent masses are apt to be crowded into the choanæ. By giving the shaft of the curette a curved or bayonet shape it is possible to avoid the obstacle offered by the incisor teeth or by the palate and thus reach farther forward in the vault (J. Fein). Other curettes are made heart-shaped, so as to actually enter the nares on either side of the septum (C. E. Munger).

Gottstein's adenoid curette.

The nasal route for reaching adenoids has been revived by Freer, who recommends for the purpose a modification of Ingal's straight nasal cutting forceps

to paint the pharynx. The best application for this purpose is a solution of 15 grains of **potassium iodide** and 12 of **iodine** in an ounce of water, well sweetened with **glycerin**. This should be applied twice a day to the pharynx with a brush, taking care to sweep the brush round with a turn of the wrist before withdrawing it, so as to reach as high up as possible behind the soft palate. This application not only checks morbid oversecretion by curing the nasopharyngeal catarrh, but also puts an end to laryngeal irritation and favorably influences the glandular enlargement. In fact, this is the very best method of treatment for acutely swollen cervical glands, and as long as the latter remain of elastic softness, varying in size from time to time according to the amount of laryngeal worry, we may expect them to be dissipated by this means. Smith (Practitioner, Jan., 1910).

Accidents and Complications.—The most serious accident is hemorrhage, which may be first shown by pallor and rapid, flickering pulse. Small children should be closely watched and not allowed to sleep continuously for several hours after operation. The contrast between the quiet and the previously noisy breathing often creates enough anxiety to enforce this caution. Bleeding usually ceases spontaneously in a very few minutes. The total loss of blood is difficult to estimate; according to C. G. Coakley, from 2 to 8 ounces is the ordinary quantity. If in excess or too long continued, measures to check it must be adopted.

An interesting and a rather promising hemostatic agent, suggested by Batelli in 1910 (**thrombokinase**), has recently been prepared by L. W. Strong in the laboratory of the Manhattan Eye, Ear and Throat Hospital. His method differs slightly from the original, and he believes he has obtained a "ferment body" fairly stable and effective in all situations where a local application is possible. It occurs in the form of crystals or scales, of which a very small quantity will promptly induce coagulation. It does not affect the caliber of the blood-vessels and is not adapted to internal use. Several members of the staff of the hospital have resorted to it in various conditions with satisfaction. As yet it does not appear to have been subjected to such a crucial test as would be offered by a case of hematophilia. Its field of usefulness is, therefore, still undetermined. It is important that the surface to which it is to be applied should be made as dry as practicable by pressure with a cotton tampon. In this particular a difficulty might be met with in the case of very free hemorrhage.

In March, 1902, the writer removed the tonsils and adenoid vegetation, at the same sitting, from a child of 11 years. The adenotomy was done with the curette of Kirstein, and the hemorrhage was not more than usual. An hour afterward it was reported that the child was losing considerable blood. A postnasal tampon was inserted; during the night a new hemorrhage developed, followed by death. The boy was suffering from leukemia of a lymphatic form.

Six months later a boy applied to Burger to have the three tonsils removed. The pharyngeal tonsil was pale, and of a cyanotic appearance, with several hemorrhagic points. Cautioned by the above accident, he first had an examination of the blood made. Leukemia was found pronounced (35 leucocytes to 400 chromocytes), and the child was placed in the medical clinic. Some weeks after, the child died, and the autopsy confirmed the first diagnosis.

The danger of fatal hemorrhage is very rare; with the exception of two or three cases of hemophilia, there are only 3 cases of fatal adenotomy reported. Burger made 2200 in the space

of nine years without the least accident. M. Burger (Revue Heb. de Laryn., d'Otol. et de Rhin., Jan. 30, 1904).

Operations upon the pharyngeal tonsils are generally considered without danger, yet wound infection and hemorrhage, although comparatively rare, do occur frequently enough to warrant careful attention. Hemorrhages may be divided into two types: those appearing at the time of operation, and those occurring some time afterward.

In the first instance the causes lie in a constitutional or a local condition, the most important of which is hemophilia. This is shown by family and personal history. If there exists absolute proof of a hemophilia, naturally the operation would be denied. But in such cases as appear relatively doubtful the operation should be given the benefit of the doubt. An unrecognized leukemia can be the cause of excessive hemorrhage. Characteristic is the livid bleached color of the tonsils. Operation in such cases can produce the same untoward results as in hemophilia. Among other diseases which impose the danger of severe postoperative hemorrhage are nephritis, heart lesions, etc., which, however, appear so rarely in cases needing adenoidectomy that they can be neglected.

Many authors have associated severe postoperative hemorrhage with the coincidence of the operation and menstruation. About 1 per cent. of cases have postoperative hemorrhage. Injury to neighboring parts, and especially the leaving of partly removed tissue shreds, are the important factors. The former more often leads to hemorrhage immediately following the operation, and only to after-bleeding when the blood-clot covering the lesion is accidentally removed. Mucous membrane shreds hanging from the wound are found in over 50 per cent. of after-hemorrhages. Hemorrhages occurring after several days generally follow sudden muscular exertion, such as sneezing, blowing the nose, etc., and are due to dislocation of the exudate covering the wounded surface. Healing had progressed so far after a week's time that bleeding is no longer to be feared. Haymann (Archiv f. Laryngologie, Bd. xxi, S. 15, 1908-1909).

Reference has already been made to the internal use of **calcium chloride or lactate** in hemophilia, as well as to local applications of the new "ferment," **thrombokinase**. Locally, instillations of **adrenalin chloride**, 1 to 1000, are sometimes effective. Direct pressure by means of a **gauze tampon** crowded up into the vault in the grasp of a postnasal forceps is usually successful. The gauze may be soaked in a saturated solution of **tannogallic acid** (1 part gallic, 3 parts tannic), one of the cleanest and most active hemostatics. Signs of collapse are to be combated by saline injections, stimulants, constricting the extremities, and similar expedients. Even after extreme exsanguination the repair of waste is generally rapid, but may need to be encouraged by the use of **ferruginous tonics** or other medication.

Such being the case, the proposal of Iglauer to transform **adenectomy** into an "almost bloodless" operation by packing the postnasal space with a tampon of rubber sponge the moment the adenoid mass has been removed is of doubtful utility. The plan suggested is like that followed in plugging the posterior nares for epistaxis. The tampon is ready before the operation is begun, and the tape attached to it is used as a palate retractor during instrumentation.

The handle of the forceps cutting laterally should not be too much depressed lest the margin of the vomer be nipped between the blades. Care should be taken to keep the blade of a cutting instrument in the middle line of the vault: if tilted to one side, there is

danger of harm to the Eustachian cushion.

A rare and interesting complication, torticollis, has been described by several writers and is probably due to sepsis or to excessive energy in the use of instruments. It disappears spontaneously in a few days and is worthy of note only because of the unnecessary alarm to which it may give rise.

Laceration of the velum would seem to be inexcusable, but has been known to occur with rough handling of an excessively large instrument, or from attempting to make use of a cutting edge in a struggling child, or before one is quite sure that the instrument has passed beyond the plane of the velum and is well within the cavity of the nasopharynx. Finally, the mucous membrane may be stripped up over an excessive area, if too dull an instrument be used, or if it be forced too deeply into the tissues. With the exception of the first-mentioned, hemorrhage, these accidents are obviously all results of faulty manipulation.

Attention has been called by Wyatt Wingrave and others to a peculiar transitory rash resembling that of scarlatina at times following removal of adenoids or tonsils. It merits notice only for the danger that it might be confounded with a more serious infectious exanthema. No precise theory of the phenomenon is propounded, whether septic or nervous, although marked leucocytosis is demonstrable for a week or ten days after. Several cases of alleged sepsis have been recorded, but in many the histories are by no means conclusive. A case of fatal meningitis, believed to be septic, has been reported by Shurly; two similar cases have been noted by Putnam, who expresses the opinion that such sequelæ are not uncommon. An interesting case of cavernous sinus thrombosis in which the surface of the basilar process of the occipital bone had been shaved off together with an adenoid mass with a Beckmann curette is a graphic warning against the use of extraordinary force (A. E. Wales). Cases of pharyngeal abscess, inflammation of the cervical glands, endocarditis, and acute rheumatism have been met with by various observers after adenectomy.

Several instances of lighting up of latent tuberculosis by adenectomy have been reported (Lermoyez, Chappell). It is perhaps more correct to say that tubercle bacilli lying in the operative field have ready admission to the circulation through the divided lymph-channels, whence general infection follows. In the majority of cases the adenoid tuberculosis is undoubtedly *secondary* to a focus in the lung or elsewhere which is excited to activity by the surgical shock of operation. In a *primary* case the results of removal are favorable (E. H. White), but there must always be difficulty in deciding this question of priority.

> The hyperplastic pharyngeal tonsil often contains micro-organisms, and these are mainly pyococcal forms. The bacteria for the most part lie near the surface, and the infection usually occurs from the surface, with or without demonstrable lesion of the epithelium. Primary tuberculosis of adenoids is probably more common than most previous studies show. Sixteen per cent. of the series contained tubercle bacilli, 10 per cent. with characteristic lesions of tuberculosis. The tubercle bacilli were present in small numbers. The lesions in primary tuberculosis of the adenoid are generally close to the epithelial surface and focal in character. Occasionally they may be found in the deeper parts of the pharyngeal lymphoid tissue. The pharyngeal tonsil

may be a portal of entry for the tubercle bacillus and other micro-organisms in localized or general infections. A. J. Lartigau and M. Nicoll, Jr. (Amer. Jour. Med. Sci., June, p. 1031, 1902).

Examination of 35 specimens of adenoids from children; in 1 case, a boy aged 3 years, suffering from caseating tuberculous glands behind the left sternomastoid the pharyngeal tonsil showed numerous tubercles. In cases of tuberculosis of the cervical glands where no other source of infection can be found the pharyngeal tonsil must be regarded with suspicion. Ivens (Lancet, Sept. 16, p. 817, 1905).

Primary tuberculosis occurs in a certain proportion of all cases of adenoids. From the figures of other observers and the author's this seems to be about 5 per cent. This is regarded as a conservative estimate. In determining the presence of adenoid tuberculosis the histological method is the most satisfactory. Tuberculosis does not appear to be an important factor in the production of adenoid hypertrophy. Adenoids and tonsils are the important channels of infection in tuberculosis of the cervical glands.

In the development of pulmonary tuberculosis adenoids may sometimes be direct channels of infection, but their importance is probably more often indirect by predisposing to catarrhal inflammations of the upper respiratory tract. E. Hamilton White (Amer. Jour. Med. Sci., Aug., p. 228, 1907).

The writer found evidences of tuberculosis in the growths in only 1 of 27 cases of adenoid vegetation, and in this case it was evidently secondary. Wikner (Hygieia, April, 1910).

An interesting case is mentioned by J. L. Morse, in which "adenoids were removed from an infant of five months during the early stage of tuberculous meningitis, tubercle bacilli being found in the adenoid tissue." The possibility of infection by this route is looked upon as a strong reason for operating in the early months of life, even with the certainty that a repetition will be called for at a later period.

Spasm of the glottis requiring **tracheotomy**, as in cases of his own, is believed by Holger Mygind to be not infrequent in adenectomy without anesthesia in rachitic children, and one should be prepared for such an emergency.

The writer has twice witnessed serious disturbance of respiration (laryngospasm with stridulous inspiration and marked cyanosis of the lips) as a result of **adenotomy** without use of chloroform. Both cases were children under 2 years having symptoms of rachitis. In the third case, in a boy of 2 years, with rachitic deformities, there was sudden collapse accompanied with suspension of respiration and cyanosis consequent to adenotomy, which required **tracheotomy.** The child's mother later declared that the child was subject to fits of suspension of respiration with cyanosis. On two occasions he had such attacks in the presence of the family doctor, and artificial respiration had to be employed. Holger Mygind (Hospitalstidende, Nov. 18, p. 1173, 1903).

Case in which a very large adenoid removed from a child aged 6 years gave rise to asphyxia on spasmodic closure of the jaw just as the child was apparently under complete ether anesthesia. The writer had to resort to **artificial respiration, hypodermic injections, forcible opening of the jaw,** and **traction of the tongue** in order to resuscitate his patient. G. L. Richards (Laryngoscope, Feb., p. 289, 1905).

After-treatment. — The control of hemorrhage, and that in very exceptional cases, is practically the only indication for interference during convalescence. If catarrhal secretion is overabundant, it is sometimes desirable to keep the parts clean with a douche or coarse spray of warm **normal salt solution.** Drainage from this region is so good that sepsis is almost unknown,

and it is well to abstain from the use of antiseptics, either in solution or powder. In order to prevent the formation of adhesions, the passage of the finger into the vault for a few days after operation has been recommended. Although no statistics on this point are available, it is believed that adventitious bands met with in adult life are due not to operative interference, but to attrition and erosion of lymphoid masses in childhood which have been neglected and have finally undergone spontaneous shrinkage.

No procedure in the upper air tract has added so much to the vigor of the race as removal of adenoid vegetations, and the fact must be admitted that they are often a source of disease, even when their volume is not sufficient to cause obstructive symptoms. Not all lymphoid nodules demand extraction: only those which are clearly causing disturbance, or inviting infection.

Removal of adenoid vegetation has brought about, in the writer's hands, recovery of 2 cases of exophthalmic goiter, 1 of glaucoma due to lesion of the fifth pair and not relieved by iridectomy, and of 1 case of Addison's disease. The persistence of the craniopharyngeal canal, the vascular communication between the pituitary cavity and the pharyngeal mucous membrane, the presence of an accessory pituitary gland encountered sometimes in the pharynx, might cause an alteration in the secretory function of the pituitary gland, and, indirectly, by intermediation of the grand sympathetic nerve and of the spinal marrow, of the other glands of internal secretion. Popp (Annales des mal. de l'oreille, du larynx, du nez, et du pharynx, Oct., 1909).

CHARLES H. KNIGHT,
New York.

ADIPOSIS. See OBESITY.

ADIPOSIS DOLOROSA; DERCUM'S DISEASE.

[The term "Dercum's disease" is that by which adiposis dolorosa is generally known in Europe. Hence its introduction here by the Editors.]

DEFINITION.—Adiposis dolorosa derives its name from its two principal features, namely, fat and pain.

[Objection may naturally be made to the form of the word "adiposis," as it is of mixed origin, being made up of a Latin root joined to a Greek termination. It has, however, the sanction of generations of use among English-speaking writers, and, besides, is paralleled by other mongrel words in common use, such as terminology, which no one any longer questions. The correct Latin form of the word would, of course, be "adipositas," the word used by German writers. However, adipositas is equally a coined word, a word artificially made, for it is not used by any Latin writer. The real Latin word is "obesitas," which, as purists, we ought to use. F. X. DERCUM.]

In 1888, the writer described the symptoms which constitute this affection in reporting a case under the title of a subcutaneous connective-tissue dystrophy. Later, in 1892, he grouped this case, a second described by F. P. Henry, and a third discovered in the wards of the Philadelphia General Hospital under the name "adiposis dolorosa," by which the affection has since become generally known. Within the next few years cases were published by Collins, Peterson, Ewald, Eshner, Spiller, Féré, and others. In 1901, Louis Vitaut (Thèse de Lyon, 1901, "Maladie de Dercum") published a special treatise on the subject. His description of the affection was so full and accurate that at the present date it needs but little modification and but few additions; the latter mainly bear upon the pathology of the affection. Up to the present

time between 50 and 60 cases have been recorded. [Among the more important recent papers upon the subject are those of Frankenheimer (Jour. Amer. Med. Ass'n, 1908, i, p. 1012), of Price (Amer. Jour. Med. Sci., May, 1909), and the thesis of Poirier, Montpelier, 1910.]

SYMPTOMS AND COURSE.—The development of the disease is usually slow and insidious. A woman who, up to the period of onset, has been well and occupied with her usual occupation notices a slight pain or tenderness in this or that portion of the body. This early symptom of pain is very variable in character and in intensity. Most often it is a sensation of smarting or stinging more or less annoying because of its persistence. Sometimes the pain, even in the beginning, is severe, though this is unusual. At other times the onset of symptoms is preceded by a sensation of cold in regions in which pain subsequently makes its appearance. As a rule, the pains at first are not very pronounced and the patient is for some time able to follow her ordinary occupation. Furthermore, the pains are not persistent, but recur at intervals, the patient being comfortable for hours and sometimes for days at a time. Little by little the pains become more pronounced, they increase in intensity and are then also accompanied by distinct local changes. The patient naturally examines the part which is painful and may note these changes herself. Sometimes there is a little flushing of the skin and sooner or later a swelling is noted. At first it is hardly appreciable, but gradually becomes more pronounced. The swelling may give a sensation to the finger of a rather firm localized edema. As a rule, it is in the beginning a small nodule,—smaller than a walnut, rarely larger. Sometimes a number of such swellings are noted at the same time. The affection continues to evolve, usually slowly; the pains become more intense and more frequent, and gradually the tumefactions change their character and finally become veritable tumors or great tumor masses. In rare cases the fatty deposit appears to make its appearance without either previous or concomitant pain, the pain making its appearance only after the enlargements or swellings have existed for some time. This, as already stated, is unusual, the most common history by far being that just outlined.

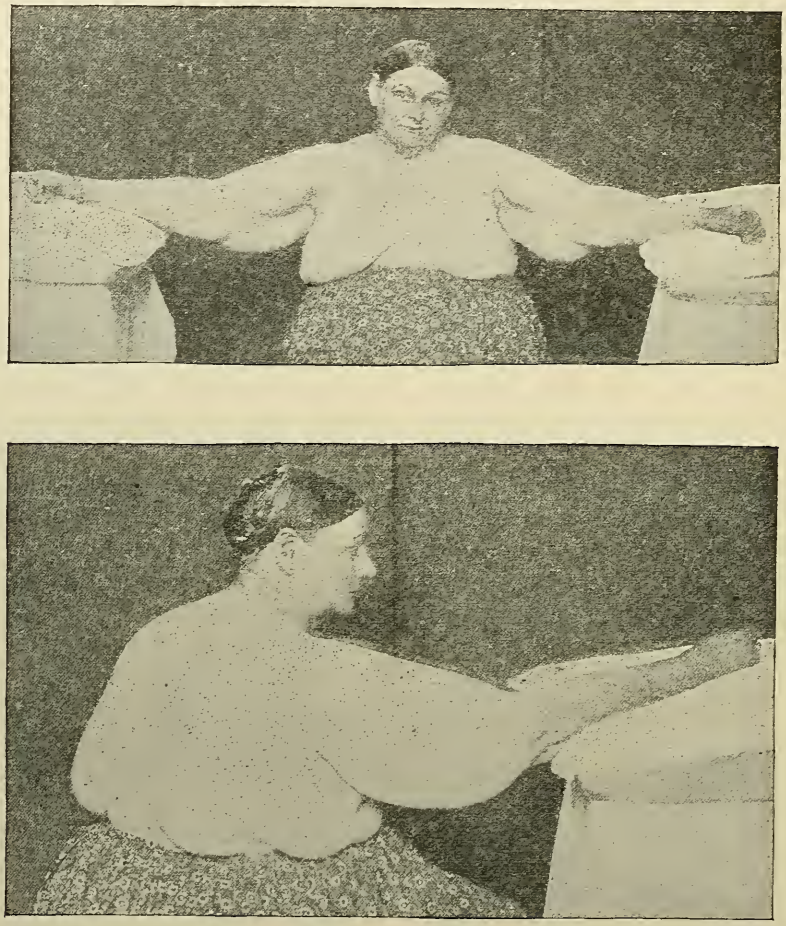
The pain is quite commonly paroxysmal, though in long-established cases it may be continuous. In the intervals the tumefactions are usually tender or painful to pressure.

When the disease is well established, we may distinguish, as pointed out by Vitaut, 4 cardinal symptoms, namely, tumor formations, pain, asthenia, and psychic symptoms.

The swellings may present themselves under three different aspects. Sometimes they are small, of variable dimensions, distinct from one another, and readily isolated. Under these circumstances they present what Vitaut has termed the nodular form of the disease. Sometimes they form extensive masses, invading an entire limb or the segment of a limb. To this condition Vitaut has given the name of "localized diffuse form." Finally, a tumor, properly speaking, may not be present, but the entire body may be augmented in volume in consequence of a hyperplasia of the fatty subconnective tissue. This condition Vitaut has called "the generalized diffuse form."

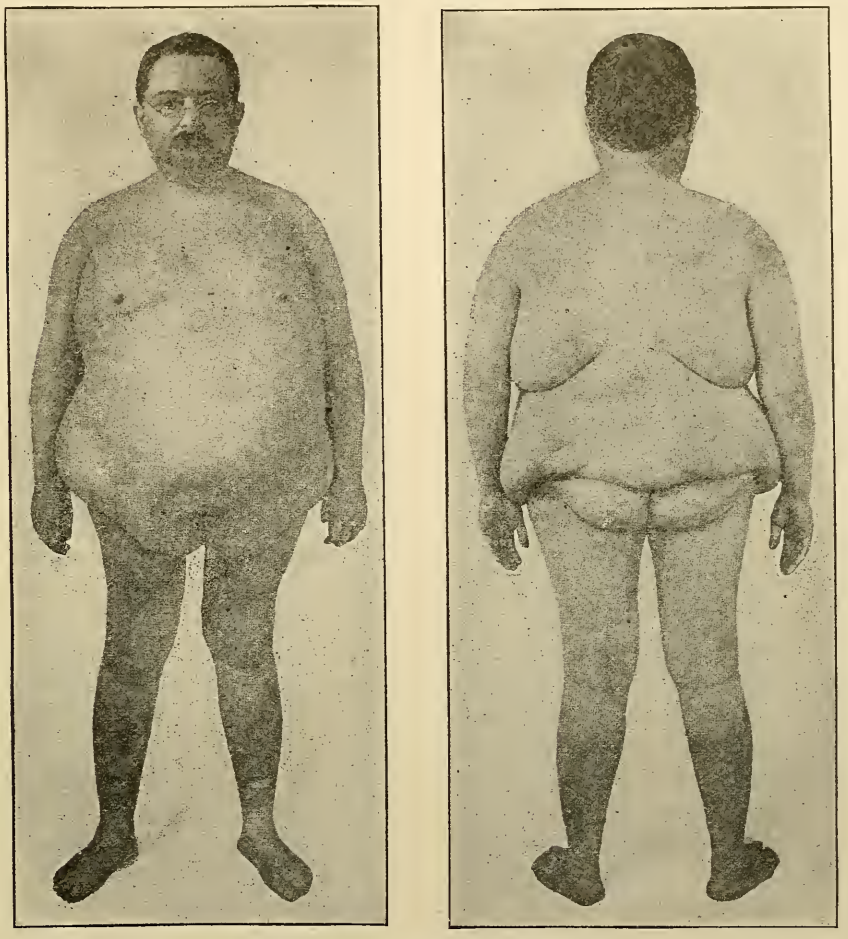
The Nodular Form.—The nodular form manifests itself at first by pains,

variable in character, stinging, itching, smarting, shooting, soon followed by a slight redness of the skin and a slight induration scarcely appreciable to the finger. If we examine the painful area, we feel a tumefaction, usually of small size, at first yielding and later a little more resistant. The sensation is that of a firm edema, which is not well differentiated from the surrounding tissue. The tumefaction appears to develop slowly in keeping with successive attacks or crises of pain. Gradually it becomes somewhat better defined, its volume increases, and its consistence changes, so that it no longer has the appearance of a simple tumefaction, but that of an actual tumor. Each increase of swelling is preceded or attended by characteristic pains. The latter are sometimes so sudden in their onset and so severe as to cause the patient to cry out. During the height of the paroxysm, the tumor may resemble very closely, in the sensation which it gives to the fingers, a "caking breast." The painful crisis having passed, it is found that the dimensions of the swelling have distinctly increased. It has become permanently larger, as well



Author's first case (*Dercum.*)

as more resistant and better defined. After repeated paroxysms, the swelling resembles a distinct tumor more and more closely. In certain portions, the mass may appear finely lobulated, while in other parts it gives to the fingers the sensation of a bag of worms beneath the skin. Each painful crisis leaves behind it very appreciable changes. In an area where nothing existed previously, we find after a crisis a diffuse edematous tumefaction; if the tumefaction has existed previous to the crisis, we find it transformed into a lobulated tumor more or less well encapsulated. Sometimes after a crisis we discover around the tumor a well-defined edematous zone, which in subsequent crises undergoes a transformation such as the original mass itself had undergone. In this way the mass may eventually attain great size. The various stages of the evolution of these masses can be followed very closely by palpation. One and the same patient, besides, usually presents in various regions tumors in various stages of development.



Case of adiposis dolorosa in a male. (*Dercum.*)

Painful crises supervene usually without appreciable cause; at times they are

provoked by trauma and at others they ensue upon unusual exertion. The patient is frequently very positive in stating that slight contusions of the surface or that excessive fatigue provokes the painful crises.

The tumors are, of course, variable in size. Some of the very smallest may be no larger than a pea, though so small a mass is the exception. More frequently the mass is of the size of a walnut or a small orange. Much larger sizes are met with. The larger masses are of course evident to ordinary visual inspection; the smaller ones require to be sought for by palpation. If we examine the patient attentively in a good light, we are struck by the changes in the skin in certain areas. In places, indeed, it presents a bluish tint due to a slight superficial veining, and if we examine such a region by the feel we frequently discover a small subjacent tumor. Small as the tumor may be, it may betray its existence by this bluish tint in the skin which covers it. It happens sometimes that these small tumors become confluent and finally form a single large mass. Such a mass gives rise to a sensation like that of a varicocele or of a bag of worms.

The masses do not appear to have a special localization; they are sometimes symmetrical in the beginning, but soon group themselves without any apparent order. They develop by preference over the limbs or in the segments of a limb. In some patients it is limited to the arms and thighs, or forearms and legs in others. Sometimes we find them on the thorax, abdomen, and lumbosacral region. The face, hands, and feet are never involved.

The relations of these neoplasms to the surrounding tissue vary according to the degree of their development. In the state of edematous swelling, they pass without exact limitation into the surrounding tissue. The skin is but slightly movable over them. Later, when they form distinct tumors, more or less encapsulated, they are mobile in all directions and the skin which covers them may be folded above them. However, they are slightly adherent to the latter, so that if one tries to displace the superjacent skin the movement is transmitted to the underlying tumor. Finally it may be noted that these masses are painful not only during the crises, but are very tender to pressure, and this tenderness, as already pointed out, may persist in the intervals between the paroxysms.

The Localized Diffuse Form.—The localized diffuse form may present itself primarily or it may develop out of the nodular form. When it develops from the nodular form, it is because the nodules multiply so rapidly that they unite and become confluent. In this way a more or less voluminous mass may develop, which involves a portion of a limb or it may be a segment of a limb or even an entire limb. However, this is not the usual method of origin of the localized diffuse form. In the nodular form the separate masses are generally so small and the evolution so slow that the patient has usually been under observation for some time before the masses become confluent. More frequently the localized diffuse form originates spontaneously and rapidly in an entire limb or a segment of a limb. In such a case the pains are felt over a correspondingly extensive region. At first the entire region presents an edematous swelling easily observable by the eye. Subsequently the evolution of the mass is substantially the same as in the nodular form. Painful crises are

here again present and the swelling increases in size with each successive attack. Finally, a mass is formed which is resistant and painful to pressure. It may be quite smooth or it may be finely lobulated, or separate, apparently encapsulated tumors may be found imbedded in the general lipomatous mass.

Naturally, in the localized diffuse form it is difficult to make out the limitations as clearly as in the nodular form. The masses involve more especially the limbs, excluding save in the rarest instances the hands, the feet, and the face; not rarely they are found on the thighs and on the back. The tumefaction may be excessively painful and may present during a crisis the sensation given by a breast distended by milk or, to repeat a term already used, a "caked breast."

The Generalized Diffuse Form.—The generalized diffuse form is much less characteristic than the nodular or the localized diffuse form. The origin and course of the affection is, however, the same. The edema may appear rapidly, even suddenly, over the greater part of the surface of the body and limbs, exclusive again of the face, hands, and feet. It increases progressively and produces a general lipomatosis. More frequently it begins in a certain part, such as the abdomen, sometimes upon one side, and then diffuses itself gradually over neighboring portions of the trunk and limbs. Other masses may make their appearance at the same time or subsequently, and, becoming confluent with the original mass and each other, a diffuse lipomatosis results. The regions affected are ordinarily the arms, the chest, the abdomen, the hips, and the thighs. Contrary to the case in the nodular and localized diffuse forms, the hands and feet are not always in this form absolutely free. At an advanced stage of the disease, it is not unusual to see small masses of lipomatous tissue over the thenar and hypothenar eminences and even on the soles of the feet. In one case the writer observed even a slight invasion of the face. Only the back of the hands and the backs of the feet escape invariably the lipomatous invasion. In consistence the swelling is resistant, but much less so than in the nodular form. The mass is spontaneously painful and tender to pressure. Sometimes the suffering owing to the universal tenderness is very great. Occasionally it is such as to prevent movement on the part of the patient and to immobilize him in his bed.

Of the three forms the most common is the nodular. It presents a special physiognomy, which makes its recognition easy. The localized diffuse form resembles certain forms of ordinary lipomatosis, but it is, notwithstanding, differentiated by the pain and other characteristics still to be considered. The pains are never absent. They are present either spontaneously or are readily elicited by pressure. Usually they manifest themselves in both of these ways. Most often they precede the appearance of the edematous swelling. Sometimes they come on at the same time as the swelling; more rarely they are not noted until after the swelling has made its appearance. Slightly marked and intermittent, they become more violent when the disease is established. The pains are described by the patients as stinging, burning, pinching, darting, or even lancinating. Most commonly they are darting and radiate or diffuse in and about the nodules. They do not follow the large nerve trunks or indeed any nerves.

The patient describes them as though they were situated in the thickness of the masses. The muscles, the bones, and joints are not painful. The pains are exaggerated or brought on by pressure or handling. If the fatty accumulation is considerable, movement and effort may increase the pain to such an extent that the patient may be obliged to remain perfectly quiet during the paroxysm or indeed continuously. There is one characteristic which one finds in all cases, namely, the paroxysmal exacerbations already described. Suddenly and without cause or following an effort or trauma the patient again feels active pain. At the same time the new formations increase in volume; if it concerns a nodule the latter is surrounded by an edematous zone more or less extended; if it is a case of diffuse swelling the skin in this region becomes more tense and the circumference of the mass increases. As the pain subsides, the swelling recedes, but never to its former dimensions. After each crisis, the volume of the new formation is increased.

All or almost all of the patients present the symptoms of a general asthenia. The patient is very readily exhausted. Even in cases in which the muscular development is good, this fact is early noted. In cases which are advanced the asthenia is very pronounced. Sometimes this is so marked that the patient is unable to leave the bed. Sometimes she is unable to change even her position in bed largely because of her weakness, but also because of the pain and the enormous increase in the size and the weight of the limbs and body generally.

The psychic symptoms are not constant. However, they are very frequently present. A cerebral asthenia or ready cerebral exhaustion is rarely absent. Many patients present in addition great irritability; this is at times so great as to be attended by a change in character and disposition. The least opposition may enrage the patient and not infrequently she will quarrel with her neighbors in the wards to such an extent that isolation becomes imperative. Sometimes she thinks that the other patients and the nurses are against her. The sleep is usually broken and disturbed by distressing dreams and nightmares. One of Eshner's patients was disturbed mentally to such extent as to necessitate her commitment to an asylum. Hale White's case had two attacks of mental disturbance. Giudiceandrea has noted delusions of persecution and a true dementia.

In several cases lessened sensibility to touch, pain, and temperature have been noted. In the writer's first case there were found areas of anesthesia, while in other areas the sensibility was diminished. The same patient complained of velvety sensations in the finger tips and in the soles of the feet. The case reported by Henry presented marked disturbances of sensation. Touch, pain, and temperature were sometimes not perceived; at other times confused. In Giudiceandrea's case the sensibility to pain, on the other hand, was much increased, especially in the regions corresponding to the adiposed masses. The thermal sensibility, again, was particularly exquisite in the regions in which there was no trace of the neoplasms. Hyperalgesia was noted by Achard and Laubry. Patients have also complained of sudden sensations of cold or heat, of formication, or of cramps in various parts of the body. Headache is not rare.

Disturbances of the special senses are quite frequent. In some observations there was noted a narrowing of the visual fields; in others various subjective sensations, such as phosphenes, muscæ volitantes; in one case amaurosis was noted, which began to disappear from the day that thyroid treatment was instituted, and in a case of the writer there was present a circinate retinitis,—a mass of partly fibrinous and hemorrhagic exudate in the center of the retina, surrounded by crescents of fatty degeneration in Mueller's fibers.

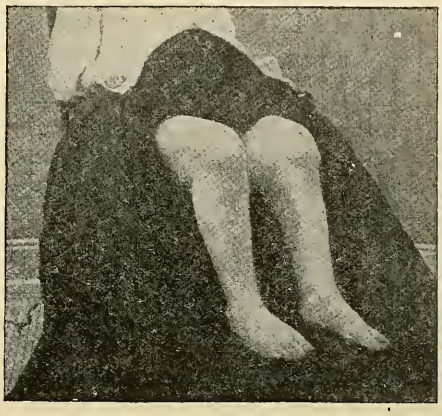
Diminution of auditory perception has been noted several times. In some cases tinnitus more or less marked has been recorded. Smell and taste were impaired in one of the writer's cases.

Vasomotor disturbances have been very frequently noted. The skin over a nodule may present no changes whatever; on the other hand, it may be noted to be somewhat injected during a crisis of pain, or much veined and slightly bluish. Occasionally the face is much flushed,—the malar regions, the frontal regions—or it may be the neck, although no actual induration or swelling accompanies the change in color.

In some cases cyanosis of the extremities and transitory edema have been noted. Frequently also the patient notices that his flesh bruises very readily, and it is not uncommon to note small ecchymoses on various portions of the limbs and trunk, and at times these evidently make their appearance spontaneously and independently of trauma. Perhaps, in keeping with this fact is the history, not infrequently obtained, of excessive menstruation or even of metrorrhagia. At times also epistaxis and, in one of the writer's cases, even hematemesis are noted.

Trophic changes in the form of ulcerations, blebs, and bullæ have been observed.

It is important also to add that there is quite commonly a marked dryness of the skin. Patients themselves comment upon this and examination confirms it.



Adiposis dolorosa with involvement of the joints. (*Dercum.*)

Among unusual complications noted in adiposis dolorosa are changes in the joints. Attention was first directed to this by Renon and Heitz, who in 1901 presented a case of "adiposis dolorosa with multiple arthropathies," before the Neurological Society of Paris. In addition to the usual symptoms of the affection there were present marked pain, creaking, and limitation of movement in numerous joints. A skiagraph of the left knee failed to reveal any alteration of the articular surface. The knee-cap, however, was a little thickened, and its structure offered a somewhat mottled appearance. The synovial membranes gave rise to a slightly opaque shadow, which was especially evident at the *cul-de-sac* under the

quadriceps tendon. This shadow, Infroit, who made the skiagraph, regarded as due to fatty thickening of the synovial membrane.

In 1902 the writer placed on record (Philadelphia Medical Journal, December 20th) a second case of adiposis dolorosa with involvement of the joints. Skiagraphs revealed no changes whatever in the bones, but some thickening of the tissues about the joints, especially about the knee-joints. The conclusion was justified that there was present a marked thickening of the synovial membranes and possibly of other structures in the neighborhood of the joints. There was a marked tendency to the formation of fringes and rice bodies. The joints appeared, as the patient expressed it, to be "loose," and motion was attended by considerable pain. That the changes observed were due, in part at least, to fatty infiltration, and that this fat was painful, just as was the fat in the tumor masses on the surface of the body, afforded the most reasonable explanation of the condition. It was possible also that an actual synovitis was present. Rheumatism could not offer an adequate explanation of the conditions found, while rheumatoid arthritis was excluded by the absence of changes in the bones and cartilages. More recently Price has made studies in the joints of two other cases confirming these findings.

A most interesting case of adiposis dolorosa in which bony changes were noted in the dorsal vertebræ and in the ribs has been placed on record by Price and Hudson (Journal Nervous and Mental Diseases, April 19, 1909). Kyphoses with corresponding deformity and reduction in size of the vertebræ were noted in the dorsal region and confirmed by the skiagraph. Similar changes were noted in the ribs. The authors call attention to the possible significance of these findings when the frequency of pituitary changes in adiposis dolorosa is borne in mind.

The course of adiposis dolorosa is essentially chronic. Its progress is slow, the patient being worse or better by turns in accordance with occurrence of paroxysms of pain. In well-established cases the suffering is continuous, subject always to more or less marked exacerbations.

In the majority of cases the patients become extremely obese, the weight often running from 200 to 300 pounds; in others again, in the nodular form, the weight may undergo only a moderate if any increase.

The symptoms may be briefly summarized as follows: fatty deposit, pain, general asthenia, and psychic symptoms. The deposits are present either in the nodular, a localized diffused or a generalized diffused form. The distinction between these forms is of course not absolute, as combinations of the various forms—or transitional states—may be found in one and the same patient. The deposits are found most commonly over the trunk, shoulders, arms, and thighs; the forearms and legs being less frequently affected and the hands and face almost never. Pain and tenderness upon manipulation of the swellings are present; spontaneous pain, pain occurring in paroxysms, is also present unless it happens that the patient is observed during an interval between paroxysms. Involvement of the nerve trunks is rare, though it has been a few times observed, not-

ably in a case of Bergerson's. Anesthesias are rare, hypesthesias not uncommon, paresthesias are frequent; the latter consist, as already pointed out, of sensations of numbness, cold, burning, tingling, crawling.

The general asthenia and the mental phenomena have been already sufficiently considered.

The tendon reflexes may be normal or increased, but are usually diminished and sometimes abolished. In one case, that of Delecq, the skin reflexes were lost. Coincident gross nervous disease has been noted several times. Hemiplegia and aphasia were noted in one case; in another, a case of the writer, a sclerosis of the columns of Goll was revealed at the autopsy, and in still another there was involvement of the lateral tracts.

ETIOLOGY. — It is occasionally noted that the patient presents a neuropathic heredity; not infrequently grave nervous disorders are noted among the ancestors or collateral relatives. Now and then it is noted that other members of the family are unusually stout, *e.g.*, in 1 of Eshner's cases the mother was obese. In a few instances adiposis dolorosa has been observed in members of the same family. Thus, Cheevers reported the case of a man whose father and sister both had the disease, while Hammond reported 2 cases occurring among sisters. The striking fact in the etiology is the predominance of the female sex; the ratio is about 6 women to 1 man. The age at which the disease makes its appearance is exceedingly variable. The youngest recorded case, that of Hale White, began at 12 years of age; the oldest case recorded was 78 years of age. According to Frankenheimer, the majority of cases in men occur between 30 and 40 years of age, and in women between 30 and 50 years.

The disease was originally believed to occur exclusively in women and about the climacteric period; although this was the rule in the writer's experience, he has known it to begin as early as 12, and has seen 3 cases in males. He describes in detail 5 cases of the affection, 4 in women whose ages range from 20 to 42, and 1 in a man aged 47. These cases all presented the characteristic symptoms of the disease. The panniculus adiposus was invariably thickened, sometimes to a marked extent. The skin was red and in dependent parts has a bluish, livid appearance. It was painful, sometimes with a feeling of burning, at other times as if it were being pierced by a needle. The skin of the legs especially, but occasionally that of the trunk and arms also, was thick and infiltrated, generally in patches, but in some cases in large areas involving the whole lower extremity except the feet. The latter condition is described by the writer as "elephantiasic edema." Actual edema was not present, the skin did not pit on pressure, and no fluid was obtained on puncturing with a needle. Charcot observed this condition in connection with individuals suffering from functional disturbances of the nervous system, and named it "œdème hystérique." Strubing (Archiv f. Dermat. u. Syphil., Feb., 1902).

Case of adiposis dolorosa, or Dercum's disease, believed to be unique, in a newborn infant. The writer was called in consultation to see the child on the day after its birth. It was then 5 weeks old, and, in addition to the characteristic irregular symmetrical deposits of fat, which were situated on the upper half of the body (the lower extremities being normal), there were two cystic formations of considerable size, one on the left posterior aspect of the neck and the other on the left breast. While lying undisturbed the child appeared to be entirely comfortable, but the slightest movement was attended with pain. W. C. Walser

(Boston Med. and Surg. Jour., June 30, 1910).

Occasionally the patient presents a history of antecedent alcoholism or of syphilis. As Price says, the toxic effects of alcoholism and syphilis are well known and the fact that they frequently cause degenerative changes in the ductless glands has been emphasized by Lorand. This is suggestive when we learn of the rôle which the ductless glands appear to play in adiposis dolorosa. In a case described by E. W. Taylor, the disease developed while the patient was convalescing from an acute alcoholic neuritis. In quite a number of cases excessive menstrual flow and even uterine hemorrhages have been noted. In one case, that of Spiller, the adiposis dolorosa followed pregnancy, while in another, that of Schlesinger, it followed an abortion. Quite a number of cases finally have developed after the menopause.

Occasionally trauma is noted in the history, and the importance of this fact has been especially insisted upon by Guidiceandrea. In a case of the writer's and in one of Eshner's, trauma seemed to be the direct exciting cause. Emotional shock has also preceded the onset, as in the case of Achard and Laubry. In Vitaut's case there appeared to be a mild infection of the digestive tract; in other cases exposure to cold and dampness, rheumatism, appeared to play a rôle. Occasionally also some other neurosis exists side by side with the affection, as in the woman reported by Henry and in a man reported by the writer, both of whom suffered from epilepsy. In other cases again, undoubted mental disease has been noted; sometimes indeed, as in one of Eshner's cases, commitment to an institution becomes necessary.

Heredity seems to play some rôle, the ancestors frequently having been obese, gouty, asthmatic, or subject to migraine; in other words, the victims of nutritional disturbances. The signs of premature senility are frequently present. M. Gilbert Ballet (Presse méd., April 8, 1903).

Case of adiposis dolorosa in a woman aged 80, the mother of 5 children, who had fallen fifteen years before, after which accident an operation was performed upon her hip, some bloody fluid being evacuated. Since that time her legs have been weak. For three years afterward, and off and on since, to her 65th year, irregular metrorrhagia existed. Pain appeared in the left hip and lumbar region, always along the nerves. It is made worse by pressure. She grew stouter very gradually, weighing now 163 pounds, while she is under 5 feet high. The fat is in large masses about the malleoli, hips, calves, buttocks, abdomen, forearms, and backs of the arms especially. This fat is only found in certain regions, and is not universally or equally distributed. Debove (Presse méd., July 17, 1901).

Case in a woman, aged 61 years, who, with an apparently unimportant family history, dates her troubles from a fall from a chair many years before the disease became manifest. The left eye became blind, and the left side of the nose developed a tumor. The adiposis appeared in her thirtieth year in the right leg first, and then in the left. The arms were next attacked. Pain accompanied all the early symptoms. When examined, the patient's neck and the subclavicular region, as well as the abdomen, besides the limbs, were loaded with fat. An enormous fatty tumor was also present on the internal aspect of the left thigh. The buttocks were immense. The pores of the skin were enlarged. Pain, lasting two or three days, in the fatty region was not uncommon. Sensation and temperature were normal; the corneal reflex was absent, as well as the patellar and Achilles. Mentality was apparently normal, but there was great asthenia, increasing with age. In view of the

eye trouble and the nasal tumor, the writers are inclined to attribute the etiology of the disease to some affection of the pituitary body. Delucq and Alaux (Presse méd., Sept. 17, 1904).

PATHOLOGY.—Up to the time of writing, eight autopsies have been held. These indicate that in adiposis dolorosa there is some disturbance of the internal secretions, excessive formation of fatty tissue, and an interstitial neuritis of the nerve-fibers contained in the deposits.

[Price has summarized the results of the various autopsies as follows:—

Cases I and II.—Dercum: Macroscopic disease of the thyroid, the glands being enlarged and the seat of calcareous infiltration.

Case III.—Dercum: Irregular atrophy of the thyroid, extensive interstitial neuritis of peripheral nerves in fatty deposits, degeneration in the columns of Goll.

Case IV.—Burr: Glioma of the pituitary body; colloid degeneration, with atrophy and absence of secreting cells in many acini of the thyroid gland; interstitial neuritis of terminal filaments; sclerotic ovaries.

Case V.—Dercum and McCarthy: Adenocarcinoma of pituitary body, thyroid normal, right suprarenal gland hypertrophied, hemolymph-glands, interstitial neuritis, undeveloped testicles.

Case VI.—Guillain and Alquier: Hypophysis doubled in size, with marked increase of connective tissue in the glandular portion and changes suggesting an alveolar carcinoma; thyroid hypertrophied, with increase in connective-tissue stroma.

Case VII.—Price: Inflammatory changes in thyroid, with marked increase in the interstitial connective tissue, one whole lobe being especially infiltrated, the other showing compensatory hypertrophy. Inflammatory changes in hypophysis, with presence of a condition suggesting alveolar or glandular carcinoma, interstitial and parenchymatous neuritis, sclerotic ovaries.

Case VIII.—Price: Marked increase in the connective tissue of the thyroid gland, dilatation of the acini, with infoldings of the cuboidal epithelial lining. The same changes in the hypophysis as were found in Cases VI and VII, but less marked. No abnormalities of the adipose tissue. F. X. Dercum.]

Delecq thinks that disease of the thyroid, testicle, ovary, and pituitary body may be causes of adiposis dolorosa. Von Schroeter concludes that adiposis dolorosa is due to a dysthyroidismus. Pineles regards the disease as a result of the disturbance of function in numerous blood-glands and that there are present hypothyroidism, genital atrophy, and changes in the hypophysis.

The thyroid gland, it will be noted, showed unmistakable changes in 7 of the 8 autopsies. These changes are very interesting and are well illustrated by the findings in the third autopsy of the writer, in which the gland was submitted to microscopic examination. A study of the sections reveals the gland to be made up of three or four different kinds of secreting tissue. In the first place, there are large acini distended by colloid material. These large acini vary in size, and their contents vary also in density. The larger acini are globular in shape, while some of the smaller ones are elongated or angular in form. The limits of these acini are clearly indicated by blood-vessels which occupy their walls. The epithelium is a single layer, which covers uniformly the peripheries of the acini. Contrasted with these there is another kind of secreting tissue, which is very solid, and in which the acini are made out with great difficulty. They consist of cells filling interspaces of the stroma, and the blood-vessels supplying these acini can only be made out in exceptional instances. The lumina of these acini when they can be made out are usually very small. There is here a

complete absence of colloid material. In other portions acini are observed which are a transition between the more solid nests of cells and the large vesicles which contain the colloid material. In addition, there is a third form of acinus, which is of peculiar interest in that the acini present plications or papillary outgrowths of the walls. These plications or outgrowths project into the lumina of the affected acini, which contain, as a rule, colloid material of lighter staining qualities than the larger vesicles, although not lighter than is contained in some of the smaller vesicles. The epithelium of these last-mentioned acini appears at times to be slightly higher than the normal cubical epithelium of the other vesicles. Finally, in some areas, solid masses of cells resembling lymphoid cells are seen, but these are probably young solid acini, like the small acini described above, though the limits of these acini are irregular, because of the absence of preserved blood in the surrounding vessels and of the absence of definite interstitial framework.

The changes observed are indicative in part of hypertrophy. Certainly this seems to be the only interpretation which can be placed on the numerous small acini which appear to be in process of development. Whether the large acini, distended with more deeply staining colloid material, are to be considered old acini, containing old or altered colloid material, it is, of course, impossible to say, but such an interpretation does not seem improbable. The plications and papillary outgrowths observed in some of the acini are also worthy of comment, in that they evidently represent an attempt to increase the secreting surface of the acini and are again expressive of hypertrophy.

These findings are very surprising, and it is difficult, of course, to frame an explanation. It is not impossible that we have here a hypertrophy which is the direct outcome of a general atrophy of the gland; in other words, a compensatory hypertrophy such as Halstead obtained in the dog after partial extirpation. The gland was small, perhaps sufficiently so to determine compensatory hypertrophy. It is probable, however, that other factors, *c.g.*, qualitative changes of function, also played a rôle in the peculiar symptoms from which this patient suffered. It is not inconceivable that as a result of deranged thyroid action some substance was thrown into the circulation, which at one and the same time prevented the proper oxidation of the hydrocarbons of the food and tissues, and also acted as a cause of neuritis and nerve degeneration. Whatever the explanation, it is interesting to recall the diminished sweating and the occasional slowness of speech and mental irritability. The interpretation is somewhat difficult; the obesity and the dryness of skin suggest thyroid deficiency, while the flushing of the face, the occasional tachycardia, and the psychic symptoms would point rather to thyroid excess, and it is safer perhaps with Pineles to regard the condition as one of dysthyroidismus.

Among the most significant findings, however, are the changes noted in the pituitary body. In 5 of the 6 cases in which the pituitary was examined, it was found diseased. Thus Burr described a glioma of the pituitary, Dercum and McCarthy adenocarcinoma, Guillain and Alquier changes suggest-

ing an alveolar carcinoma and Price changes likewise suggesting alveolar or glandular carcinoma in 2 cases. The detailed findings in the case of Dercum and McCarthy are very interesting.

The pituitary body was closely adherent to the dural lining of the sella turcica, and an attempt at removal of the gland revealed a calcareous layer from 1 to 3 mm. in thickness, between the dura and the gland substance. When this was removed, what appeared to be the normal portion of the gland occupied the left quarter of the mass; the remaining three-fourths consisted of a tumor mass. It was of the same consistence as the gland structure, roughened on the surface where the calcareous plate had been removed, and attached at its farthest end to the internal carotid artery.

The calcareous plate under the microscope showed a true bone reticulum infiltrated with the eosinophilic cells comprising the tumor mass. Sections were made transversely through the gland and tumor. The tumor mass was composed almost entirely of the eosinophilic type of cells, arranged irregularly, with a minimal amount of interstitial tissue. Around the periphery of the tumor mass the cells were arranged in parallel rows, much after the type of cell arrangement seen in endotheliomata. The tumor mass had, on account of the arrangement of the cells in rows at its periphery, an appearance as if it were encapsulated and separated from the normal gland tissue. A careful study of the cells of the tumor revealed no trace of a regular arrangement of the cells, such as is seen in the acini of the normal gland. The individual cells were round, stained a pinkish red with eosin, and contained a small, deeply staining nucleus. The nucleus in some of the larger cells was very large and irregular in shape, such as is frequently seen in proliferating cells. The cells varied greatly in size: some were twice the size of the normal gland cells; others one-third to one-fourth that size. Between these cells, and at times in the capillary vessels of the tumor mass, small areas of colloid material were seen.

The area of normal gland tissue—*i.e.*, arranged according to the normal gland structure—is about one-third the size of the normal adult gland, and is situated between the tumor mass and the protuberance, consisting of cerebral tissue. The larger portion of the glandular acini is perfectly normal. At the junction of the latter with the nerve tissue, and extending into the latter area, are large groups of cells, following an alveolar arrangement and differing from the rest of the section by the deep staining properties of the cells with nuclear stains. The posterior portion of the gland, composed of reticular nerve tissue, is permeated by the small, round, deeply staining nuclei in such a way as to give the impression that the infiltrating process followed definite lymph-channels. At the periphery of the acinous portion of the gland, masses of colloid material, of sufficient size to be visible to the naked eye as minute dots, are inclosed in areas lined by rounded cells. The tumor mass, composed as it is of the same type of cells as make up the acinous portion of the gland, must necessarily belong to the carcinomata. The infiltrating tumor formation, beginning in the acinous portion of the gland and involving the cerebral portion of the gland, follows the cell arrangement of an adenocarcinoma. The arrangement of the eosinophile cells of the tumor mass

around the periphery of the tumor resembles an endothelioma, but the type of cell points strongly to a diagnosis of carcinoma.

In commenting upon the involvement of the pituitary in the above instance, the writers pointed out, that bearing in mind the interrelation which exists between the thyroid gland and the pituitary body, the pituitary body is thus brought into relation, though perhaps indirectly, with a fat-producing or fat-destroying function—a relation which, up to that time, had not been considered. In the light of recent observations this subject assumes a new importance. Froelich has shown that, instead of the symptom-complex termed acromegaly, lesions of the hypophysis may be associated with an adipositas universalis and genital atrophy. In other words, hypopituitarism, other things equal, leads to adipositas. Further curious and remarkable interrelations of function—seemingly antithetical—appear to exist between the pituitary and the pineal gland,—the pineal gland appearing to have a fat-producing and a fat-destroying function inversely to the pituitary. For a detailed presentation of the subject, which here would lead us too far afield, the reader is referred to Otto Marburg's interesting paper on "Adipositas Cerebralis," a Contribution to our Knowledge of the Pathology of the Pineal Gland," Deutsche Zeitschrift für Nervenheilkunde, 1908, Bd. 36, p. 114.

In his discussion of the pathology of adiposis dolorosa, Price points out that sufficient attention has not been given the pituitary, which, he suggests, is etiologically of almost as much importance as the thyroid. It would appear, indeed, from the above considerations that the pituitary must be seriously considered, and he asks the question whether the symptom of adiposis dolorosa may not result from primary disease of either the pituitary or the thyroid gland. It is well known that a close interrelation exists between these two glands; experimental extirpation of the thyroid in animals has been found to be followed by pituitary enlargement and it would seem that disease of one gland means sooner or later disease of the other. Poirier also directs especial attention to the hypophysis, which he evidently regards as the most important structure concerned in adiposis dolorosa.

An examination of the fatty deposits reveals not only the structure of fatty tissue, but also the signs of great nutritional activity. Fragments removed during life by the Duchenne trocar in the writer's first case and submitted to microscopical examination presented the appearance of a connective tissue embryonal in type. The cells were voluminous, fusiform and containing large nuclei, while the intercellular spaces were filled by a transparent substance apparently without structure. On the whole the appearance was that of a lymphoid tissue. In some fragments fat cells were numerous and among these were cells which evidently had not undergone complete fatty transformation. In some of them the nuclei were still very apparent, while osmic acid revealed fat drops suspended in the cell contents.

In the autopsy recorded by Dercum and McCarthy, the fatty nodules were submitted to microscopical examination with the following result. Each of the larger nodules was composed of capsules inclosing large numbers of small, oval, fatty bodies connected with each other and with the capsule by delicate

fibrous bands. These delicate trabeculæ united and joined thick, jelly-like bands attached to the capsule. Sections made through the connective-tissue capsule and the fatty bodies *in situ* gave the following structure: The capsule was composed of several layers of well-developed connective tissue. Within this capsule a looser areolar tissue is met. This tissue is highly vascular, and between the vessels is a reticular tissue, denser in some areas than others and inclosing a large number of mononuclear cells, a few polynuclear cells, and large numbers of cells staining a tawny color by the Van Gieson stain. Scattered through the granular, tawny masses many of the mononuclear type of cells may be found. In other areas granules of blood-pigment in clumps may be seen. Wherever the connective-tissue trabeculæ penetrate into the congested fat nodule, this same fine, reticular structure, holding in its meshes rich plexuses of blood-vessels, and between these a fine reticulum of connective tissue filled with a light-yellow granular material, with nucleated yellow cells, small mononuclear cells, polynuclear reagents, as do nucleated red blood-cells, and numbers of degenerating red blood-cells, may be seen. Some of these cells react to many of the staining corpuscles, but to the Biondi-Ehrlich triple stain they appear more as mononuclear leucocytes. This tissue is identical in structure with the hemolymph-glands found in the immediate neighborhood of the large, congested nodules of subcutaneous fat.

Lying loose in the yellow fat, several small, firm bodies, the size of a split pea and of a yellowish-brown color, were found. These proved on microscopic examination to be hemolymph-glands. They were composed of a capsule of connective tissue, from which trabeculæ of connective tissue spread in many different directions throughout the body. Within this trabecular network a rich plexus of capillaries was found. Between the capillaries a fine meshwork of fibers contains large numbers of lymphoid cells, with here and there groups of red blood-corpuscles. Free blood-pigment giving the iron reaction was found in small quantities free in the trabecular network. The

Fatty nodule dissected from subcutaneous fat; shows the encapsulation of the fat, with nerve-fibers branching over it. (*Dercum and McCarthy.*)

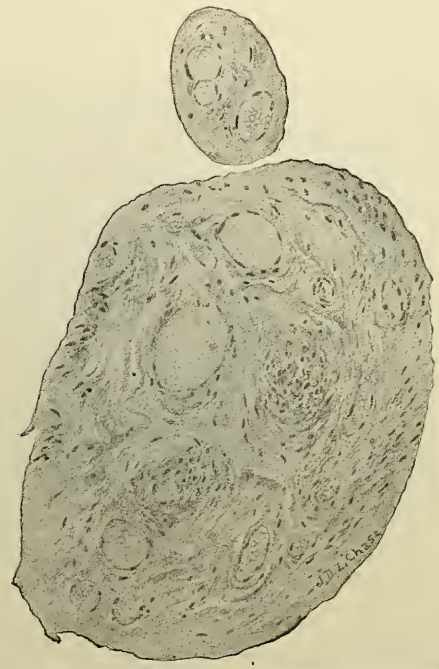
opinion of Dr. Simon Flexner that these structures are new-formed hemolymph-glands was confirmed by that of Dr. A. S. Warthin, of Ann Arbor, who has written on the subject.

An examination of the nerves found in the fat has shown the presence of an interstitial neuritis. There is a diminution of nerve-fibers, together with a marked proliferation of the perineurium and endoneurium. (See illustration, next page.)

The chemistry of the subcutaneous fat was investigated by Edsall, who especially sought for an increase in the fatty acids as this might have had to do with the pain and tenderness.

However, marked free acidity was not present. Its amount was rather low, lowest of all in the tumor fat, and decidedly below that of normal fat. The significance of this fact is not evident.

Case in which there concurred adiposis dolorosa with well-marked myxedematous manifestations. In view of the frequency of myxedematous symptoms in adiposis dolorosa, we are justified in accepting a kindred cause of both syndromes. That thyroid insufficiency stands at the foundation of myxedema there can be little doubt; again, some thyroid alteration was found in 4 out of 5 cases of adiposis dolorosa which came to autopsy. While the seat of the externally visible pathognomonic symptoms of myxedema is in the subcutaneous tissues, that of adiposis dolorosa is situated in the fatty structures.



Section of nerve in subcutaneous fat nodule showing interstitial neuritis. A distinct overgrowth of connective tissue is present between the nerve-fibers. The number of blood-vessels is also increased over normal nerve-tissue. (*Dercum and McCarthy.*)

Moreover, the improvement of case reported following the administration of thyroid extract seems to evince with certainty that perverse thyroid function was, to say the least, an antecedent. The yielding of both symptom-complexes to the same medication again points to their interrelation or their springing from a kindred cause. Thyroid therapy cannot, therefore, be utilized as a test of differentiation between myxedema and adiposis dolorosa, as some authors maintain, because both syndromes may vanish under its influence, and, as in the present instance, even at the same time. In so far as the pains disappeared in the ratio of shrinkage of the fat bunches, we are justified in concluding that the irritation of the nerve terminals was either due to mechanical insults on the part of the overgrowth of fat-tissue or to certain fatty acids or products of catabolism exciting the nerve trunks in the vicinity of the fat deposits and stimulating the fat-tissue to further proliferation. In view of the fact that myxedema occurs without pains in the swellings, it appears that thyroid insufficiency cannot be held directly responsible for the aches and paroxysms in adiposis dolorosa. Heinrich Stern (Amer. Jour. Med. Sci., March, 1910).

DIAGNOSIS.—The diagnosis is based upon the presence of the fatty masses, presenting the feature of pain, spontaneous, paroxysmal, or elicited by manipulation, and having in addition the physical peculiarities already described. The disease is readily differentiated from myxedema because of non-involvement of the face and hands and because of the absence of pain in myxedema. When the tumor masses are numerous and small, they might suggest neurofibromatosis, but the peculiar character of the swellings, the fact that they appear lobulated under palpation, that they are spontaneously painful and almost never occur upon

the face or hands would serve to make the differentiation.

In neurofibromatosis, again, there are two kinds of tumors, some of them cutaneous, not rarely on the face, and others on the mucous surfaces. They are of soft, yielding consistence and very slightly painful. Others, those of nervous origin, are small, very hard, and often grouped along the course of the nerve trunks like a string of beads. They are only laterally mobile, while the adipose tumors are mobile in all directions and are irregularly distributed. Again, anomalies of pigmentation are rare in adiposis dolorosa, but are frequent and sometimes very pronounced in neurofibromatosis. On the whole, it is hardly probable that an error could be made.

In simple obesity, the fat is distributed throughout all the tissues and does not heap itself up in separate lipomatous masses, such as is the case in adiposis dolorosa,—even in the so-called diffuse form. Besides, ordinary obesity is painless and is a matter of gradual development, while the fatty deposit in adiposis dolorosa is painful and occurs as the result of successive crises.

PROGNOSIS.—Adiposis dolorosa is an affection which is essentially chronic. Most cases live for many years and it does not appear to immediately threaten life. However, in cases of long standing, a bed-ridden period eventually ensues; general exhaustion becomes more and more marked; degeneration and failure of the heart muscle, pulmonary congestion, or a renal complication may terminate the picture. The resistance to infection also appears to be greatly diminished, for one of the writer's cases died very rapidly of an attack of erysipelas.

Cases in a relatively early stage of development—more particularly cases with small nodular or localized and limited deposits—offer a distinctly better prognosis and are distinctly amenable to improvement. Advanced cases, cases with very extensive deposits, marked asthenia, and especially with the tendency to subcutaneous hemorrhages and hemorrhages from the mucous membranes are very unpromising.

TREATMENT.—In the treatment of adiposis dolorosa one remedy has in a few cases proved of value and that is **thyroid** substance. This should be given in doses of from 2½ to 5 grains three times daily, for a very long time. The **salicylates**, notably **aspirin**, are of decided value in relieving the pain. The best plan of procedure, as a matter of course, is to place the patient in bed, and to institute a systematic course of treatment. The **rest** should be absolute and should extend over several months of time.

> Typical case with symptoms of myxedema in which the treatment consisted of an antiobesity diet, **thyroid** medication, and physical therapeutics, especially **vibratory massage** and **exercise.** Nine months later the patient presented herself to show the beneficial effects of the treatment. Excepting the pallor, which, she said, had always caused her much annoyance since her early youth, she looked very well. She felt strong, and was able to walk from five to eight miles a day; she experienced no shortness of breath on ordinary exercise, but perspired mildly when she walked briskly. The fat bunches had disappeared almost entirely; the neuralgic pains had ceased about four months earlier; there was no tenderness on pressure on the location of the former

fat masses. The skin in the supraclavicular regions and in the face had been quite tender. She evinced not the slightest mental depression and apathy, but, on the contrary, displayed a healthy optimism. Her weight had been reduced to 161 pounds. Heinrich Stern (Amer. Jour. Med. Sci., March, 1910).

The patient should be weighed when treatment is begun and thyroid substance given at first in small and then in somewhat larger doses. At the same time a **diet** should be instituted that is largely free from carbohydrates and fats. It should be remembered, however, that a diet, no matter how rigid, will of itself make no impression in adiposis dolorosa; it will fail absolutely. It is of course wise to institute a careful diet, but patients do better when the diet is not too strict. Inasmuch as the affection is attended by a marked asthenia, the diet should be nutritious. It should consist of the red meats in moderation, the white meats freely, the succulent vegetables, eggs, and skimmed milk. The latter can be used between meals and if necessary also at mealtimes.

The pains are not infrequently controlled or at least made better by **aspirin** or **salophen** in full doses, 10 or 15 grains three times daily after meals. Sometimes the tenderness and soreness are better borne when the limb or part affected is gently supported by a flannel roller; if the tenderness be extreme a layer of cotton-wool may first be applied.

Just as soon as the tenderness permits, **gentle massage** should be instituted; sometimes this can never be employed; in other cases again it can be instituted comparatively early and there can be no doubt that in a measure it favors the diminution of the swellings, especially if the patient can bear deep kneading. **Bathing between blankets** as in ordinary rest treatment should also be carried out, but of themselves baths accomplish nothing in adiposis dolorosa; indeed the physical exertion and manipulation attendant upon the application of ordinary hydrotherapeutic measures in these cases exhausts the patient.

It is a good plan to keep a record of the pulse and temperature during the thyroid administration, although the writer has never observed any fluctuations of moment in these cases, even when the thyroid was pushed. The patient should, of course, be weighed from time to time and the dose of thyroid modified according to the impression made. In some cases no impression whatever can be made; in other cases again the impression is decided. In 3 cases of the writer, the result was most satisfactory; 2 of these were treated systematically by rest in bed; the third could not for certain reasons be put to bed. In all 3 the improvement in the size of the swellings and in the lessening of pain was very great. Treatment was carried out six months to a year. In 1 case the affection recurred at the end of two years, but was again controlled. In the second, improvement and practically good health has persisted for four years. The third was greatly improved and has disappeared from observation.

The experience of the writer with cases in the hospital wards and outpatient departments has been very unsatisfactory partly because many of the cases were greatly advanced, the deposits being enormous and the asthenia grave, and partly because

the cases could not be kept systematically under treatment for a sufficiently long period.

General tonics, iron, arsenic, strychnine may be given, but they do not help appreciably. Electricity is useless. Finally, it would in the judgment of the writer be perfectly justifiable to attempt the surgical enucleation of a specially painful mass; this procedure has not yet been attempted. We should bear in mind, of course, that these patients have but a feeble resistance to shock and often present, even to superficial examination, marked cardiac weakness.

F. X. Dercum,
Philadelphia.

ADIPOSITAS CEREBRALIS. See Obesity, Fröhlich's Disease.

ADNEPHRIN. See Animal Extracts: Adrenals.

ADONIS VERNALIS.—Adonis is a ranunculaceous plant, closely related to the anemone, growing wild in Europe, Asia, and Africa. Several species of adonis are employed,—*Adonis vernalis, A. æstivalis, A. capensis, A. cupaniana,* and *A. amurensis,*—but all seem to possess the same properties, although the several varieties are variously employed in the different countries in which they grow. In Russia, for instance, it has long been employed in cardiac diseases, and in Africa as a substitute for cantharides, the bruised leaves, when fresh, possessing vesicating properties.

DOSE.—An infusion of 4 to 8 parts of the plant in 200 of water may be given in tablespoonful doses three or four times a day (Huchard). The tincture may be administered in doses of ½ to 1 dram (2 to 4 c.c.). The fluidextract has also been used in doses of 1 to 2 minims (0.06 to 0.12 c.c.).

Cervello isolated a glucosid from *Adonis vernalis,*—adonidin,— a yellow, hygroscopic powder having a bitter taste, obtained from the leaves. It is soluble in water and alcohol, but insoluble in ether or chloroform. Adonidin is administered in doses varying from 1/16 to ¼ grain (0.004 to 0.017 Gm.). It acts more promptly than digitalis.

Inoko also obtained a glucosid—adonin—from the Japanese plant, *Adonis amurensis.* This substance is free from nitrogen, amorphous, colorless, of a bitter taste, and soluble in water, alcohol, and chloroform. The effects observed on the heart of a frog were precisely those seen when digitalin is used. It is about twenty times weaker than the adonidin obtained from the European *Adonis vernalis.*

PHYSIOLOGICAL ACTION.—Adonis resembles digitalis in its action upon the heart when given in therapeutic doses. It increases cardiac energy and raises the arterial tension. The increased contractions eventually diminish and a period of quiet follows, varying in duration with the dose administered.

The prevailing knowledge of the mode of action of adonis is based on experiments with the glucosid adonidin. The results have, on the whole, been contradictory. While Cervello and Lesage found that it arrested the heart in systole, Huchard and Hare ascertained repeatedly that this organ was arrested in diastole and Guirlet found the left ventricle in systole and the other cavities in diastole. There has been greater concordance in

respect to its effects on the blood-pressure, all observers having found that there was first a rise, then a fall.

While the primary slowing is attributed to the inhibitory action of the vagus, since its section prevented it, Hare found that the diastolic arrest was not due to this nerve, since it occurred after the latter was divided, while galvanization of the nerve later on also failed to inhibit the heart. He concludes, therefore, that adonidin tends secondarily to paralyze the vagus—Kakowski, in fact, found that it caused dilatation of the coronaries instead of contraction of these arteries. Hare's experiments indicate that it may also cause primary stimulation and secondary paralysis of the vasomotor system.

Adonis has been credited with diuretic properties by Bubnow, Altmann, and Michaelis, though their observations have failed to be confirmed by certain others. Whatever diuretic power it may have is probably the result of activation of the renal circulation (Wood).

[Viewed from my standpoint, the evident confusion which attends prevailing knowledge concerning the action of adonidin is due to the fact that all these experiments, which are of many years standing, do not take into account facts I have since pointed out (see "Internal Secretions," vol. ii, 1907): (1) That the inhibition of the heart is due not to true vagal fibers, but to vasomotor fibers which the vagus contains and transmits to the coronaries; (2) that the caliber of the cardiac arterioles is governed by sympathetic fibers, and (3) that the secretion of the adrenals takes part in cardiac dynamism.

If now adonidin is considered as a *stimulant of the adrenal and sympathetic centers,* instead of as a depressant of any center, the action of the drug becomes plain: by exciting the adrenal center it increases the production of adrenal secretion, and thus causes the preliminary rise of blood-pressure while strengthening cardiac action. A larger dose excites, besides, the sympathetic center, as this center governs the caliber of the cardiac arterioles, the heart muscle receives less blood and its contractions weaken then cease, with failure of the circulation as a normal result—all irrespective of the vagus, which does not contain sympathetic fibers.

This enables us to explain, also, why some experimenters observed that the heart was arrested in systole, while others found it stopped in diastole. These results are contradictory simply because the preparations differed chemically. Those which produced arrest in systole, the better drugs, excited more actively the adrenals, and the excess of adrenal secretion caused such violent contractions of the heart muscle that the organ finally failed to dilate (the tetanic or cramped heart); on the other hand, the poorer drugs excited more actively the sympathetic center, and, the cardiac arterioles being unduly constricted, the heart muscle failed to receive enough blood to sustain its contraction and the heart remained dilated, *i.e.,* in diastole. S.]

INCOMPATIBILITIES. — The glucosid adonidin in solution is decomposed by free acids or alkalies. It is incompatible with tannic acid, corrosive sublimate, and silver nitrate. The physiological incompatibilities of adonis include aconite, amyl nitrite, muscarin, veratrum viride.

CONTRAINDICATIONS.—Adonis is contraindicated in arteriosclerosis, in affections attended by a high vascular tension (as in the earlier stages of interstitial nephritis), and in hypertrophy and other disorders of the heart in which digitalis, its physiological homologue, is harmful.

THERAPEUTICS.—Adonis is useful in cases of valvular heart disease with loss of compensation and in which evidences of grave circulatory disorder, such as cardiac asthma, are present. It

has been specifically recommended in **aortic** and **mitral regurgitation**. The diuretic powers of the drug cause it to be of value in cases of **dropsy** and **cardiac degeneration**. It is also valuable in **palpitation** dependent upon irregular inhibition. As it does not seem to possess cumulative tendencies, it may be administered with more freedom than digitalis. According to Dujardin-Beaumetz, however, large doses cause gastric disorders and vomiting. Borgiotti found adonis valuable in different **cardiac disorders**. One dram to 1 ounce of the infusion daily constitutes an excellent cardiac tonic. In **fatty degeneration of the heart** it increases diuresis and regulates the circulation.

> The writer found the drug very useful in many conditions as a substitute for digitalis, though its action is weaker; but it has the advantage over digitalis of being free from disagreeable by-effects, especially effects of a cumulative character. It is, therefore, appropriate for long-continued use, when, for some reason, the administration of digitalis is undesirable or inadvisable. A satisfactory form of employment is a 1.5 to 2 per cent. infusion, which may be prepared by the patient himself, and the dose of which is a tablespoonful every two hours. Mutterer (Therapie d. Gegenw., Oct., 1904).

Adonidin is credited with properties superior to digitalis, in that it acts more promptly and with less tendency to cumulation. As Dujardin-Beaumetz had observed in the case of the infusion of adonis, however, Lublinski and Durand have found adonidin to produce violent gastrointestinal disorders with diarrhea and vomiting. According to Dujardin-Beaumetz, the dose should never exceed ⅓ grain (0.02 Gm.); Huchard gives 1/12 grain (0.005 Gm.) three or four times daily in adults.

[The therapeutic value of adonis or adonidin would be unquestionable and in reality exceed that of digitalis were we able to obtain a reliable product. This is especially true in view of the fact that the so-called "cumulative" action of digitalis is due, from my viewpoint, to its tendency to excite the sympathetic center, while a good preparation of adonis or adonidin does not possess this defect. S.]

As a remedy for the reduction of **obesity**, adonis æstivalis has proved of value. Owing to the fact that it does not possess a tendency to cumulation, it may be continued for a long time. It is claimed to have been effective in relieving the heart from an excessive covering of fatty tissue. The tincture of this species may be given in doses of 10 minims (0.6 c.c.) three times daily.

> Case in which the patient weighed 342 pounds and suffered severely from dyspnea when the administration of adonis was begun. After taking 10 drops of the tincture three times daily for twelve days there was a loss in weight of 17 pounds, the respiration had become easier, and there was general euphoria. R. Kessler (Amer. Medico-Surg. Bull., Aug. 15, 1894).

To reduce the active cerebral hyperemia present during a paroxysm of **epilepsy** adonis has been recommended, owing to its power of stimulating the vasoconstrictors. It may be advantageously combined with the bromides.

[There is good ground for the belief that adonis is a valuable remedy. By exciting the adrenal center it enhances general metabolism, and simultaneously the conversion of the spasmogenic wastes into eliminable products, thus preventing the fits. It was used with success by Bechterew and others. S.]

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ADRENALIN. See ANIMAL EXTRACTS: ADRENALS.

ADRENALS, DISEASES OF THE.—Although it is the purpose of this Cyclopedia to present the prevailing or current views upon the subjects treated, the writer does not feel that he can conscientiously observe this rule in the present instance. Having probably devoted more time to the study of the ductless glands and to a comparative analysis of the work done by others than any other investigator in this comprehensive field, he does not hesitate to state that the physiological rôle authors in general now attribute to the adrenals, though correct as far as it goes, represents only *a part* of the functions these organs actually carry on in the body. To be more explicit, he cannot admit that the functions of the adrenals are, as stated even in recently published textbooks, merely to raise the blood-pressure and give tone to the muscular elements of the heart and blood-vessels; he maintains that, *besides* these well-known properties, the adrenals sustain tissue oxidation and metabolism by contributing an oxidizing ferment to the hemoglobin, and that they also take an active part in the autoprotective process known as "immunity," the active agents of which, notwithstanding the great amount of work devoted to the subject, have never been traced to their original source.

[It is impossible within the limits of an encyclopedic article to review at length the physiological evidence upon which these four correlated functions are based. It may be recalled, however, that the action of the adrenal secretion on the heart and blood-vessels was first pointed out by Oliver and Schäfer in 1894, while their rôle in oxidation, general immunity and fever was pointed out by myself in 1903 in my work on "The Internal Secretions and the Principles of Medicine," the fourth edition of which has recently (1911) appeared. The conclusions of Oliver and Schäfer based on relatively simple experiments have become classic, while mine, which required experimental investigations from many directions, physiological, biochemical, clinical, etc., by a correspondingly large number of investigators, may be said to have been steadily gaining ground.

The action of the adrenal secretion on the blood-pressure and cardiovascular system discovered by Oliver and Schäfer being familiar to every one, I will submit only a summary of the fundamental features which sustain my own view concerning their additional influence upon general oxidation, including metabolism, immunity, and fever:—

The Adrenal Secretion in Pulmonary and Tissue Oxidation.—The prevailing diffusion doctrine as to the absorption of oxygen from the pulmonary air and the elimination of carbonic acid, having been shown by Paul Bert, Müller, Setschenow and Holmgren, Bohr and other authorities to be defective, Bohr concluded in 1891 that some internal secretion capable of taking up the oxygen from the air in the lungs was necessary to explain the process. A comprehensive study of the question led me to the conclusion that it was the internal secretion of the adrenals which carried on this all-important function. The following are but a few of the main factors in support of this opinion:—

1. *The marked affinity of the adrenal secretion for oxygen,* sustained by the experimental observations of Vulpian, Cybulski, Langlois, Battelli, Abel, Takamine and others, including the writer.

2. *The presence of the adrenal secretion in the venous blood between the adrenals and the pulmonary air cells,* sustained by the experimental observations of Gottschau, Manasse, Aulde, Stilling, Pfaundler, Cybulski and Scymonowicz, Biedl, Langlois, Dreyer, Salvioli and Pizzolini and personal anatomical researches.

3. *The marked reducing power of the blood coursing in the walls* of the air-cells, shown by the experiments of Robin, Verdeil, Garnier, and Müller.

4. *The presence in the hemoglobin, of a constituent whose physicochemical properties are those of the adrenal secretion,* sustained

by the observations, first, of Vulpian, Gautier, Moore, Moore and Purinton, and Cybulski as to the properties of the adrenal principle; those of Battelli, Dixon and Young as to the presence of the adrenal principle in the blood; of Mulon as to its presence in the red corpuscles; of Schmiedeberg, Jaquet, Abelous and Biarnès, and Salkowski, and my own as to the presence of an oxidizing ferment in the blood; of Jolles and Poehl as to the catalytic and oxidizing properties of the adrenal components of the blood.

5. *The presence of the hemoglobin containing the adrenal principle in all parts of the body, including the skin,* sustained by the presence of melanins everywhere and their identity as hemoglobin derivative and as the adrenal principle based on the investigations of Leonard Hill, Hirschfeld, Chittenden and Albro as to melanin being an hemoglobin derivative; those of Boinet, Mühlmann, and myself as to the identity of melanin (the bronze pigment of Addison's disease) as a product of the adrenals.

6. *The marked influence of the adrenal secretion and preparations upon the temperature, general oxidation, and metabolism,* sustained by the observations of Reichert, Morel, Lépine, Israel, and others, including myself, as to their ability to cause a rise of temperature; those of Brown-Séquard and many others, as to the steady decline of temperature following removal of the adrenals, or occlusion of the adrenal veins; the hypothermia of Addison's disease; the observations of Byelaventy, Ioteyko, Dessy and Grandis, and others, including myself, as to the increased gaseous interchanges and cellular metabolism, and the increase in the elimination of waste products caused by the adrenal principle.

The Adrenal Secretion in Immunity.— The adrenal secretion in this connection is, from my viewpoint, but *one* of the antibodies which carry on this process, being what has been termed by Bordet the "fixative" or "specific immunizing body" and by Ehrlich "amboceptor." Referring to "Internal Secretions" for details which cannot be embodied here, upon this phase of the question, I will limit myself to the direct relationship of the adrenals with the autoprotective functions:—

The adrenals are known to carry on antitoxic functions. Sustained by the observations of Albanese (1872), which showed that removal of the adrenals reduced the resistance to poisoning by neurine; those of Abelous and Langlois (1892-1898), which showed that the adrenals neutralized poisonous substances derived from muscular activity and bacterial products, and also by the investigations of Mosse. Additional testimony is afforded by the marked evidences of overactivity shown by the adrenals under the influence of certain waste products and toxins, as noted by Langlois and Charrin, Petit, Stilling, Auld, Wybaux, and others, and also by the protection afforded by adrenalin injections against strychnine injections observed by Oppenheim, Meltzer and Auer and various toxemias and infections as observed by Hoddick, Netter, Marran and Dare, Moizard, Kirchheimer, and many other clinicians.

The relationship between the adrenals and general oxidation, shown above, also establishes a connection with the production of *fever,* which, in the light of modern work is also considered, up to a certain limit, as a defensive process. C. E. DE M. S.]

To disregard functions of such importance would make it impossible to account for many phenomena awakened by disorders of the adrenals, and correspondingly limit our usefulness in the practical field. This entails, however, the necessity of granting to the adrenals a position in pathology equal to any of the major organs. Indeed, the functions I have attributed to them, in addition to those with which they are already credited, entitle them to rank pathogenically with the heart and blood-vessels in so far as the general vascular pressure is concerned, and the lungs in respect to respiration and tissue oxidation.

When, moreover, their rôle in the autodefensive or immunizing processes of the body is also taken into account, their importance may almost be said to exceed that of other organs; since they thus not only serve to sustain life through tissue oxidation, but also to

protect life through their rôle in immunity.

CLASSIFICATION.—Impairment of these functions to any extent, through factors which either inhibit or exaggerate the secretory activity of the adrenals, must necessarily awaken symptoms which indicate the functional disorders present. In Addison's disease (treated by Prof. Langlois, of Paris, on pp. 356-374 of this volume), for example, where destruction of the adrenals or of their secretory nerves by a local lesion correspondingly compromises their functions, we have as main phenomena not only the vascular hypotension and cardiac weakness which the well-known action of the adrenal secretion on the blood-pressure explains, but also the low temperature, the general coldness, the dyspnea and the gradual emaciation which deficient oxidation alone accounts for. Now if, from any cause, the functions of the adrenals are inhibited, we have a reproduction, more or less marked according to the degree of inhibition, of these morbid phenomena. They form the symptom-complex of the condition which appears to me best designated by the term "hypoadrenia."

[This term was selected owing to its greater exactness and brevity than "hypoadrenalism," and owing to the fact that the latter suggests the presence of a habit such as "alcoholism." It is obviously less cumbersome than "insufficiency of the adrenals" or "adrenal insufficiency," and corresponds with terms in current use such as "anemia," "asthenia," etc.

In 1899 Sergent and Bernard (Archives Générales de Médecine, July) were the first to advance the view that adrenal insufficiency was a syndrome due to destruction of the adrenals, but standing apart from Addison's disease, which they ascribed mainly to lesions of the abdominal sympathetic. My own researches ("Internal Secretions," vol. i, 1903, and ii, 1907) sustained the opinion of many other observers, however, to the effect that the elimination of Addison's disease was not warranted, and that this disease presented the most comprehensive external picture of gradual destruction of the adrenals or of the periadrenal sympathetic structures, or of these structures and the adrenals jointly, *i.e.*, of adrenal insufficiency.

Again, Sergent and Bernard ascribe the syndrome of adrenal insufficiency as a whole to a general intoxication which they divide into fulminant (sudden death), acute (rapid autointoxication), and subacute (slow autointoxication). From my viewpoint, however, all the symptoms excepting the convulsions are due to the inhibition of functions which are primarily dependent upon the adrenals: viz., general oxygenation, metabolism, and nutrition. The only intoxication phenomena, the convulsions witnessed in these cases, I ascribe to the accumulation of toxic wastes (shown by Abelous and Langlois to be antagonized by the adrenal secretion) which are not broken down with sufficient rapidity when the oxidation processes sustained by the adrenals are inhibited. C. E. DE M. S.]

Of the various forms of hypoadrenia is one which is practically unrecognized, though frequently a cause of death, mainly among children, viz.:—

TERMINAL HYPOADRENIA.

DEFINITION.—Terminal hypoadrenia is a form of marked asthenia which occurs late in the course of an acute febrile disease as a result of exhausting secretory activity of the adrenals—acting as defensive organs—in the course of that disease.

[The term "terminal" is inserted here because it is important to differentiate this form of hypoadrenia from that which occurs early in the course of a toxemia and known as adrenal hemorrhage, treated farther on in this article. C. E. DE M. S.]

PATHOGENESIS AND SYMPTOMATOLOGY.—The adrenals being admittedly concerned in the protection of the organism during infections and intoxications, by contributing an excess of their secretion during the

febrile stage of the disease (sometimes considerably prolonged), it follows that, after this stage is over, the adrenals should lapse into a condition of more or less temporary insufficiency through fatigue or exhaustion. That other organs concerned in the immunizing process are influenced in the same way must doubtless be the case, but the fact remains that it is the symptomatology of hypoadrenia that is uppermost.

In lobar pneumonia and bronchopneumonia, for instance, resolution may be considerably delayed and convalescence likewise. There is, late in the case, extreme adynamia and a low blood-pressure, the temperature is below normal, the pulse weak and more or less rapid, and death from heart-failure is not infrequent. In typhoid fever, hypoadrenia is commonly observed. The disease assumes what is now known as the cardiac type, with, late in the case, extreme prostration, a rapid, weak and sometimes irregular pulse, hypothermia, and a marked tendency to vertigo, fainting, and cardiac failure.

[Sicard (Bull. de la soc. méd., July 21, 1904) reported the case of a young woman in whom the foregoing symptoms appeared on the ninth day of a bronchopneumonia. Extreme muscular weakness, marked hypothermia and low blood-pressure, diarrhea, and Sergent's white line, which denotes marked adrenal insufficiency, were present. On the fifteenth day the blood-pressure fell to 70 or 80 (7 or 8 per cent. potain) and death followed three days later. At the autopsy the adrenals were found hemorrhagic. This suggests that adrenal lesions may be present in all such cases. Yet, Ribadeau-Dumas and Bing (Bull. de la soc. anat., June 3, 1904) have witnessed the same symptoms in cases of measles which recovered, while Bossuet (Gaz. hebd. des sci. méd. de Bordeaux, Oct. 30, 1904) refers to 8 cases in various febrile disorders in which typical symptoms of adrenal insufficiency, asthenia, low blood-pressure, etc., developed suddenly and disappeared spontaneously, aided perhaps by adrenal extract which had been administered.

As stated recently by Morichau-Beauchant (Le progrès médical, Oct. 9, 1909), the adrenals seem to show a special predilection for certain infections. Diphtheria easily leads them all in this connection. So seriously do these organs suffer in these cases that Sévestre and Marfan have termed the type "secondary syndrome of malignant diphtheria." Hutinel ascribes the fulminating cases of scarlatina to this cause. Tetanus, erysipelas, mumps, certain forms of tonsillitis, and certain streptococcic infections may also present the typical syndrome of hypoadrenia. Goldzicher (Wiener klin. Woch., June 10, 1910) was led by his researches to conclude that in the various forms of septicemia the appearance of lower blood-pressure was to be ascribed to insufficiency of the adrenals. C. E. DE M. S.]

When, at the end of an infectious disease, the case, instead of proceeding to convalescence, remains in a condition of asthenia, with low blood-pressure and temperature, there is good ground for the conclusion that terminal hypoadrenia has occurred. Exhaustion of the adrenals during the acute process having inhibited the secretory activity of these organs, the above symptoms result from inadequate oxidation of, and metabolic activity in, the tissues. Sergent's white line, brought about by gently rubbing a narrow streak over any part of the abdomen with the finger, may be obtained in the majority of these cases. After a short period the area becomes whitish and remains so a short time.

The writer announced in 1903 that he had occasion to observe a condition simulating meningitis in a young girl, but autopsy revealed complete cheesy degeneration of both suprarenal capsules, while the meninges were intact. A white line appeared when the fingernail was drawn across the abdomen of the patient, and lasted for two to five minutes. He

has since noted this white line in a number of other cases in which the suprarenals were primarily or secondarily affected, and others have confirmed his observation. The writer has never observed it with an arterial pressure above 13 (Potain—130 mm. Hg). It disappears on administration of adrenalin, and is evidently due to reflex spasm of the capillaries during low arterial tension, with more or less dilatation of the vessels. The subject was discussed at the meetings of the Paris Société Méd. des Hôp., in February, at which some cases of the suprarenal pseudomeningitis were reported, as also two cases of insolation in which the white line, or a partially red line, was noticed. In both these cases lumbar puncture, with removal of 20 c.c. of fluid, had a marked beneficial effect, especially on the headache. The fluid was comparatively normal, but under considerable tension. Sergent (Jour. Amer. Med. Assoc., Apr. 20, 1907).

The writer has critically examined the significance of Sergent's sign in 79 cases, taking the blood-pressure in all of them with Potain's sphygmomanometer. The white line was present in 31 patients, absent in 41, and intermittent in 7. In 2 patients with definite lesions of the suprarenals, as proved by autopsy, the sign was absent. In the 31 cases in which the sign was positive the blood-pressure was low in 8, normal in 7, high in 11, and variable in 5; in the 41 cases in which the sign was negative the blood-pressure was high in 22, normal in 8, low in 8, and variable in 3. He concludes that this white line is not a sign of suprarenal insufficiency and is not dependent on low blood-pressure. L. Bernard (Bull. et mém. Soc. Méd. d'Hôp., Paris, vol. xxiv, p. 866, 1907).

The writers found the white line present in 145 out of 228 cases; 65 of these had hypotension and 80 a normal or hypertension. The 83 cases which did not give the test included 30 with hypotension and 53 with normal or hypertension. The 80 cases with the white line without hypotension and 30 with hypotension without the white line make a total of 110, or one-half of the 228 cases tested, which do not conform to the rule. They conclude that the white line cannot, therefore, constitute a sign of either adrenal insufficiency or hypotension. Lautier and Grégoire (Soc. de biol., vol. lxvii, p. 690, 1910),

The patient complains of chilliness; the surface is pale, owing to the poverty of the blood in cellular elements and hemoglobin, and to recession of the blood-mass from the surface to the deeper vascular trunks. The vascular tension being low, the pulse is rapid and the heart-beat weak. Anorexia, due to deficient metabolism and diminished demand for food, nausea, the result of relaxation of the gastric muscular coat, and diarrhea, due to a similar condition of the muscular coat of the already passively engorged intestine, and more or less frequent fainting spells, are all concomitant symptoms that may be witnessed in such cases, which are always greatly exposed to relapse or to sudden death from heart-failure.

The writer published with Bernard a description of this syndrome in 1899. He now reports 2 more cases with necropsy which corroborate the existence of a pseudomeningitis originating in suprarenal insufficiency. There had evidently been a chronic affection of the adrenals in each case, clinically latent, until fanned into a flame which proved rapidly fatal. One patient was a young woman, the other a man of 32. The symptoms suggested intoxication from the sudden suppression of the suprarenal functions. The syndrome may simulate, also, acute dyspepsia, poisoning, peritonitis, or cholera. The combination of pains in the epigastrium, anorexia, vomiting, extreme prostration and progressive emaciation, arterial hypotension and tachycardia indicated the suprarenal origin, but other

signs such as instability of the pupils, photophobia, pain on pressure of photophobia, and pain on pressure of the eyeballs, cutaneous hyperesthesia, a plaintive cry and tardy headache, indicated meningitis, notwithstanding the absence of contractures, of Kernig's sign, and of the meningitis stripe, with the retention of consciousness. The necropsy disclosed that there was no meningitis, but merely a pseudomeningeal reaction, a suprarenal encephalopathy. Sergent (Presse méd., ii, No. 94; Jour. Amer. Med. Assoc., Jan. 2, 1904).

The author has observed nine cases of acute suprarenal insufficiency or variable intensity, ending in recovery. The symptoms develop very rapidly, and, besides, they can disappear spontaneously, at the same time with the illness which they accompany, for this acute adrenal insufficiency is due to an infection or an intoxication. The writer has always noted that the insufficiency occurs in the course of a toxic or infectious malady, medical or surgical. The longest duration of this acute suprarenal insufficiency that the writer has observed was one month and a half, in a woman who was suffering from an outbreak of syphilis. This affection has yielded to the employment of adrenal extract. The patients treated by the author recovered from the suprarenal insufficiency in a few days. In eight of the nine patients the cure appears to be definite, for the symptoms, which disappeared with the causal illness, have not returned after an interval of several months. In one case of recurrent bronchitis, however, with every attack, the patient became asthenic and the skin became dark. But when the attack of bronchitis passed, so did the insufficiency. It would be very difficult to say to what lesion of the capsule the syndrome corresponds. The fact that this insufficiency is secondary to an intoxication or infection is the characteristic which gives it a true clinical importance. G. Bossuet (Gaz. hebd. des Sci. Méd. de Bordeaux, Oct. 30, 1904).

Case of acute insufficiency of the adrenals in an apparently healthy farmer who had been doing some hard work, exposed to the sun for several hours, when suddenly he collapsed with intense abdominal pain and headache, with great prostration. On the presumptive diagnosis of sunstroke, he was treated with cold to the head and purgatives, but the symptoms persisted, soon accompanied by vomiting and hiccough; the prostration increased, with a tendency to stupor; there were intense headache and delirium, respiration was superficial, the pupils were dilated and did not react to stimuli, the heart-sounds became faint and death occurred at the end of the week. The only pathological findings at autopsy were atrophy of the adrenals from a sclerotic process in the veins, and compression from a hematoma from rupture of one of the veins in the adipose tissue surrounding the left suprarenal capsule. The writer attributes the acute insufficiency in his case to excessive exposure to the heat of the sun. Sotti (Policlinico, Jan. xv, Med. Sec. No. 1, 1908).

Symptoms arising in the course of scarlatina which are very suggestive of insufficiency of the suprarenals. The symptoms are asthenia, depression, failure of the heart-power, hypotension of the arteries, tendency to syncope, abdominal pains, and a brown coloration of the skin. The use of small doses of adrenalin had a remarkable effect in the cases cited, the patient recovering after being in an apparently desperate condition. V. Hutinel (Le bull. méd.; Med. Record, Sept. 18, 1909).

Complications of various kinds may occur. The immunizing processes being greatly weakened through the deficiency of adrenal secretion, one of its important factors, septic infection, abscesses, bone lesions, tuberculosis of a rapid type, and other infections may more or less rapidly develop. Disorders of nutrition, cholelithiasis, and occa-

sionally Addison's disease may also appear. In acute pulmonary infections, pneumonia, for example, organs in the neighborhood of the focus of infection, the pleura, the mediastinal glands, etc., being inadequately protected by the blood or its phagocytic cells, become the prey of specific bacteria. Briefly, the body is rendered vulnerable to the attacks of almost any pathogenic organism.

PATHOLOGY.—In the special type in question no adrenal lesion may be discernible. In the majority of instances, however, the organs are enlarged and congested and may show, here and there, a limited hemorrhagic area. Their appearance suggests not only the functional torpor incident upon functional exhaustion, but the presence of a *passive* congestion resulting from loss of resiliency of their sinusoidal vessels, thus impeding the circulation through them. Occasionally they are the seat of suppuration, a complication which is apt to be observed when the causative disease is, or includes, a streptococcic infection, pneumonia, or meningitis.

> The functional disturbance in the adrenals during disease estimated by the lesser pressure-raising power of the extract in various animals. It showed that the adrenals are not materially affected by various pathological conditions, starvation, fever, etc., but that others, such as uremia, phosphorus poisoning, diphtheria, and various infectious processes, apparently arrested the suprarenal functions. The extract of the organs under these conditions failed to display the normal pressure-raising property. F. Luksch (Wiener klin. Woch., Bd. xvii, Nu. 14, 1905).

The pathological picture of the more severe form of adrenal complications, *i.e.*, intercurrent *hyperadrenia,* shows far more distinct lesions of the adrenal parenchyma. Hence the typical lethal phenomena that attend many of these cases.

> Case of infarction of the right adrenal which would appear to be almost unique, as no mention of such a condition is made in the literature referred to by Rolleston in his lectures on the suprarenal bodies. Specimen obtained from the body of a female child, aged 11 months, who died from some throat trouble, possibly diphtheria. On opening the abdominal cavity a mass of the size of a goose-egg, and resembling a hematoma, was found in the right renal region. It was found that the right adrenal was imbedded in this mass; it was enlarged and firm, but very dark, almost black, in appearance, as from hemorrhage. On section the lines of the cortex and medulla could be seen with difficulty, and the entire substance of the gland was of practically the same consistency and dark color. In the medullary portion, and corresponding to the site of the central vein, was a large, round, whitish mass, in size about that of an ordinary match, which had all the appearance of a thrombus. This could be followed throughout the length of the organ. The left adrenal showed some hemorrhagic spots, both in the medulla and cortex, but otherwise was healthy. Woolley (Jour. of Med. Research, Mar., 1902).

Mott and Halliburton have found already that in cases of death from exhausting diseases the adrenalin present in the adrenals was diminished or absent. The writers have extended these observations; they have examined the adrenals in the cases of 50 adults dying from various diseases. The glands were placed in Cohn's fluid for twenty-four hours and afterward stained with Scharlach or Sudan III; by this method the chromaffinic substance and the fat were demonstrated. They relied upon this demonstration of the amount of chromaffinic granules in

the cells of the medulla, and did not carry out the physiological test. No appreciable loss of the substance occurred during twenty-four hours following death, as told by control experiments in animals. Adrenalin was always being given off, especially if the splanchnics were stimulated. The conclusions drawn from their work were that in cases of acute infection and rapid death adrenalin was absent in the medulla; this applied also to cases of death from shock and from peritonitis when, in short, the blood-pressure was low. On the contrary, in chronic diseases, such as phthisis, adrenalin was to be found in the medulla. In cases of high blood-pressure adrenalin was present and distinctly increased. F. A. Bainbridge and P. R. Parkinson (Brit. Med. Jour., Mar. 11, 1907).

In 25 experiments on guinea-pigs and hedgehogs, the writer found that in only three was the microscopic condition of the adrenals approximately normal, while in the remaining 22 very characteristic changes were present, which in 18 were of serious degree, consisting of hemorrhages and necroses, alone or combined, after poisoning with the diphtheria toxin. Strubell (Berl. klin. Woch., March 21, 1910).

TREATMENT.—In these particular cases the use of **adrenal gland,** or of **pituitary body,** which acts very similarly but with less violence and more lasting effects, sometimes gives surprising results. The adrenal product—which, from my viewpoint, is also the main active agent in the neural lobe of the pituitary, as shown by the chromaffin test—supplies precisely what the body needs, *e.g.,* the resumption of all oxidation processes (thus restoring general metabolism and nutrition), and a rise of blood-pressure, which causes the blood to circulate normally in all organs, including the skin and the adrenals themselves. Indirect effects are also obtained: its action on the heart increases the contractile power of this organ, which is thus rendered capable of projecting the blood with more vigor through the lungs, and causes oxygenation of the blood to become more perfect. Recovery is also materially aided by the rise of blood-pressure that the adrenal product insures, causing, as it does, arterial blood to be driven from the splanchnic area toward the peripheral organs, including the lungs and the brain. From these features alone considerable benefit is derived.

If we recall, moreover, the participation of the adrenal secretion (which the adrenal preparation administered represents) in the immunizing process, we have the added factors of ridding the blood of any intermediate—and therefore toxic—wastes, bacterial toxins, etc., it may contain, and of increasing phagocytic activity, thus antagonizing efficiently any pathogenic organism that may remain to compromise the issue.

Thus explained, we can understand the phrase, "little short of marvelous," applied to the results obtained by some clinicians. We can also understand the marked reduction in the mortality obtained by Hoddick (Zentralbl. f. Chir., Oct. 12, 1907) in cases of peritonitis following appendicitis accompanied by uncontrollable decline of the blood-pressure, cyanosis, and other evidences of collapse, and also in puerperal toxemias, by the slow intravenous use of adrenalin in saline solution. Hoddick ascribes the lowering of the blood-pressure to paralysis of the vasomotor center; but as the toxemia is the cause of this condition, an agent capable of counteracting both cause and effect is necessary. This is met by the adrenal principle. Josué (Soc. Med. des Hôpitaux, May 21, 1909), in typhoid fever, likewise relieved threatening symptoms by

injecting 15 minims (1 c.c.) of **adrenalin** (1:1000 sol.) in ½ to 1 pint (250 to 500 c.c.) of physiological **saline solution** subcutanously. The influence of the saline solution in these cases must not be overlooked, however. Eight years ago I urged that death was often due, in infectious and septic diseases, to the fact that the osmotic properties of the blood became deficient, and advised the use of saline solution *from the onset* of the disease. The reduction in the mortality of pneumonia in the practice of men who have carried out this suggestion has demonstrated its value.

[Several clinicians have employed much larger doses of the adrenal active principle with profit. Marran and Darré (Jour. des praticiens, May 15, 1909) found it of great value in the collapse of diphtheria with marked asthenia, low blood-pressure, and subnormal temperature. Moizard (Revue de thérap., Jan. 1, 1910) recommends adrenal organotherapy as soon as asthenia and low blood-pressure occur in any infection. He gives daily two sheep's fresh adrenals, finely divided and mixed with powdered sugar, or administers the active principle, 10 to 20 drops daily divided in five or six doses. Kirchheimer (Münch. med. Woch., Dec. 20, 1910) has found large doses, 10 to 24 minims, safe hypodermically in the collapse of pneumonia, diphtheria, and scarlet fever. Letulle has found it of great value in the latter disease. The better plan, from my viewpoint, is to inject it with saline solution (at 108° F.), intravenously, the needle of the syringe containing the adrenalin being inserted into the rubber tube of the saline solution apparatus. C. E. DE M. S.]

Adrenal organotherapy is useful both for differentiation and cure, and the writer has witnessed the entire subsidence of the Addison syndrome, including the disappearance of the "white line" under the influence of suprarenal medication. Fresh glands from young calves may be used, the patient ingesting from 1.5 to 2 Gm. a day up to 5 Gm., or the dry extract can be taken. This is kept up for ten or twelve days, then suspended for two or three, and then recommenced. As a rule, he prefers the extract of the whole gland, but he sometimes uses adrenalin. He has found this particularly useful in infectious disease when he suspected suprarenal involvement. Signs of cardiovascular weakness subside under the influence of the adrenalin, and the white line vanishes and reappears parallel with the fluctuations of the pulse, which he regards as substantial proof of its pathognomonic character. The usual dose is 0.001 Gm. a day, but up to 0.006 may be given fractioned in six doses, and this may be kept up for two months. E. Sergent (Presse méd., July 10, 1909).

Case of adrenal insufficiency due to typhoid fever in a woman of 46 years. The symptoms: low blood-pressure, tachycardia, a persistent feeling of coldness, marked asthenia and lassitude, tendency to syncope, vomiting, stubborn constipation, marked anemia, and emaciation, lumbar pains radiating throughout the abdomen, continued five months. **Adrenal organotherapy,** of all the remedies tried, was alone of value, the symptoms recurring as soon as it was stopped, to again disappear when the use of adrenal medication was resumed. After five days the patient was able to rise; the convalescence proceeded regularly under the influence of the remedy. Fortineau (Gaz. méd. de Nantes, Feb. 28, 1910).

[In this case, the adrenals had probably become the seat of organic lesions in the course of the febrile process which had reduced their functional efficiency to a marked degree, the adrenal secretion produced being inadequate to raise general oxidation and metabolism to the needs of convalescence. Hence the almost immediate effect (noted the next day) produced by addition of the adrenal principle to the blood through organotherapy. C. E. DE M. S.]

Collapse of obscure origin sometimes occurs in the course of infectious diseases. This accident, which not infrequently ends fatally, is explainable by lesions of the adrenals. The success obtained with glandular extracts in such

cases affords evidence in favor of this view. The adrenals, when active, exert an angiotonic and antitoxic action, and suppression of their functions results in phenomena akin to those of fatigue. In infections complicated by adrenal insufficiency hemorrhages into these organs have often been noted. If severe and bilateral, such hemorrhages result in death. In the slowly progressing forms of adrenal failure, treatment by glandular extracts is also of great value. Such treatment is indicated as soon as asthenia and lowered blood-pressure appear. The author recommends the daily administration of two capsules of fresh **suprarenal substance** from sheep, finely divided and mixed with powdered sugar, or, better, the use of **adrenalin** solution (1:1000) or of cachets containing glandular extract. In children 10 to 20 drops of the 1:1000 solution may be given daily, divided into five or six doses. Moizard (Revue de thérap., Jan. 1, 1910).

If adrenal insufficiency arises during the progress of diphtheria, the writer advises combining **suprarenal opotherapy** with **serotherapy.** If syphilis is also present, suprarenal opotherapy may be associated with mercurial treatment. In the other infectious diseases, where no specific medication exists, opotherapy should be begun from the beginning of the symptoms of suprarenal insufficiency. **Adrenalin** may be given by the mouth, or, if the hypodermic method is used, 1 c.c. of a 1:1000 solution is added to 50 grams of normal **salt solution** and injected into the subcutaneous tissue. As this medication is inoffensive, it can be continued daily until the accidents of suprarenal insufficiency have disappeared. Comby (Archives de méd. des enfants, Jan., 1911).

These measures are only indicated in emergency cases, however. In the average case the **glandulæ suprarenales siccæ** of the United States Pharmacopeia, administered by the mouth, is fully as effective if a good preparation is obtained as soon as asthenia and low blood-pressure appear. The powder in 3-grain (0.2 Gm.) doses, three times daily, in capsules, gradually increased until 5 grains are given at each dose, usually suffices. When the cardiac adynamia disappears, a small dose of **thyroid,** the desiccated gland, ½ grain (0.03 Gm.); **strychnine,** 1/60 grain (0.001 Gm.), and **Blaud's pill,** 1 grain (0.06 Gm.), added to each capsule, greatly hasten convalescence. The iron and the adrenal product serve jointly to build up the hemoglobin molecule, a slow process when left to itself.

For our knowledge of the action of the use of pituitary extracts in infectious diseases we are mainly indebted to L. Rénon and Delille (Bull. de thérapeutique, Feb. 8, 1907), who began their use in 1907. In a recent work in which the clinical observations of both observers are recorded, Delille ("L'Hypophyse et la médication hypophysaire," 1909), referring to grave cases of typhoid fever, states that they showed "arterial hypotension, irregularity of the pulse (especially the grave forms), oliguria, insomnia; while convalescents showed asthenia, hypotension, or at least 'effort hypotension' (Oddo and M. Achard), paroxysmal or continuous tachycardia"—all, we have seen, symptoms of hypoadrenia or adrenal insufficiency. They found 1½ grains of **pituitary extract** (of both lobes) at noon daily extremely efficient; it counteracted at once the depressed arterial tension, produced diuresis, counteracted insomnia, and greatly improved the general condition. Similar effects were observed in diphtheria and erysipelas. The results in pneumonia do not appear to me to warrant the use of any adrenal or pituitary preparations early in the case, the first few days of the disease, when the blood-pressure and the fever are high. They should be used *only when a low*

blood-pressure and other symptoms of hypoadrenia are present. The results reported by Delille strengthen this opinion. In advanced tuberculosis no beneficial effect was observed.

ACUTE HYPERADRENIA AND ADRENAL HEMORRHAGE.—This condition, which may lead to fatal hypoadrenia by arresting the functions of the adrenals, is generally known under the term of "adrenal hemorrhage." The association with hyperadrenia, *i.e.,* excessive functional activity of the adrenals, introduced here, is important in that it calls attention to the cause of the lethal hemorrhage, viz., *abnormally high temperature and blood-pressure.*

[Just as *hypo*adrenia appears to me to replace advantageously "hypoadrenalism" and "adrenal insufficiency," so does *"hyper*adrenia" seem to convey more exactly excessive adrenal activity than "hyperadrenalism," which suggests habitual overactivity, besides being less cumbersome than the phase "excessive secretory activity" and others in general use. C. E. DE M. S.]

This disorder is, briefly, the result of undue activity of the adrenals. Hyperemia of these organs occurs normally, *i.e.,* physiologically (owing to their participation in the autodefensive functions of the body), in the course of all febrile infections or intoxications. When these toxemias are severe this adrenal congestion is increased in proportion—sufficiently so in some instances to cause rupture of the adrenal vascular elements, and hemorrhage within the organs. An additional cause of congestion in the latter is the abnormal rise of blood-pressure which the unusual production of adrenal secretion entails; all the vessels of the body being unduly contracted, the adrenal capillaries, which are deprived of muscular elements, are overladen with blood and prone, therefore, to rupture. These few facts are necessary to elucidate the definition of the disorder.

DEFINITION.—Acute hyperadrenia is that condition of the adrenals characterized by intense congestion of their vessels, which occurs in the course of severe febrile infections and certain intoxications, and manifested by a high blood-pressure, and in infections, also, by a high temperature. When this congestion exceeds the resistance of the adrenal vessels adrenal hemorrhage occurs, causing death when both adrenals are hemorrhagic, in a large proportion of cases, especially infancy and childhood.

[The limitation "certain intoxications" is introduced, because active congestion of the adrenals is produced only by poisons which cause a marked rise of the blood-pressure, strychnine and quinine, for example. As shown in "Internal Secretions" (vol. i, pages 19 to 55, 4th edition, 1911), the use of such remedies in the course of infections and intoxications may do harm by increasing the congestion of the adrenals and therefore the chances of hemorrhage. C. E. DE M. S.]

SYMPTOMATOLOGY AND PATHOGENESIS.—This disorder is relatively common in children, especially in infants; death occurs, from adrenal hemorrhage, without premonitory symptoms, except, perhaps, a hemorrhagic rash or purpura—denoting excessive vascular tension—over the body, and a high temperature. The toxemia here has promptly destroyed the adrenals. As a rule, however, more or less marked phenomena, besides those due to the disease from which the child may be suffering, and varying considerably with each case, initiate this acute phase of the process, the adrenals being on the border-line of hemorrhage. These may include vomiting and diarrhea, melena, very acute abdominal pain, hematemesis, icterus, fever, with hyperpyrexia

sometimes immediately before the adrenal rupture. When the hemorrhage occurs there is more or less sudden collapse, a very feeble and rapid pulse, shallow respiration and, perhaps, some bronchial rhonchi, the face being more or less dusky, cyanosed, or even livid, and the temperature subnormal. These phenomena are typical of adrenal insufficiency or failure, the adrenal secretion sustaining, we have seen, general oxygenation and metabolism and cardiovascular contractility.

Still (Pathol. Soc. Reports, 1898), who collected the cases recorded up to 1898, divided them into three groups:—

1. Those in which death occurred within a few hours or days of birth (never later than the sixth day), *i.e.*, cases of congestion or hemorrhage in the suprarenals in the newborn.

2. Those in which death occurred later, and the suprarenal lesion was a complication of some disease, usually of the respiratory tract.

3. Those in which, after an acute illness lasting only two or three days, usually with a purpuric or bulbous eruption, death occurs, and the suprarenal lesion appears to be part of the fatal disease.

To this latter group belongs a case recorded by Voelcker (Registrar's Reports, Middlesex Hospital, 1894), in which an infant, aged 2 years, died with acute illness and purpura, and was found to have hemorrhage in both suprarenal capsules. This association of suprarenal hemorrhage with acute illness and purpura is seen also in the cases recorded by Garrod and Drysdale and Andrewes (Pathol. Soc. Reports, 1898), and in a recent case at the Royal Free Hospital (Post-mortem Reports, 1900). Andrewes considers that we have clearly to do with an infective process, and inasmuch as several cases have occurred in unvaccinated children, the question of variola deserves consideration. Probably, however, the association is merely an accident owing to the occurrence of death in infancy. Talbot's cases were both infants with a history of sudden onset of vomiting, abdominal pain, convulsions, a temperature of 100° or 101°, and nothing discoverable to account for the symptoms; purpura, however, was not present. In the Royal Free Hospital cases there was some evidence of acute bronchial inflammation. Still considers that the association with a respiratory disease, producing severe dyspnea and cyanosis, suggests an asphyxial origin for some of the cases that occur in later infancy. Talbot (St. Bartholomew's Hospital Report, 1900).

Symptomatology of adrenal hemorrhage as observed in 80 cases: (1) In 46 out of 79 cases there were no appreciable signs. (2) In 5 cases there was a voluminous hematoma or abdominal tumor that could be perceived by palpation. The diagnosis was made in 1 case only during life. (3) There were peritoneal symptoms in 6 cases, all accompanied by tearing of the capsule with hemorrhage. (4) There were symptoms of capsular insufficiency in 8 cases. (5) In 15 cases there was sudden death, or death after three days at the most, sometimes accompanied by delirium, convulsions, contractures, coma, hypothermia, and syncope. In more than half of the cases, therefore, the hemorrhages remain latent and apparently without effect upon the organism. F. Arnaud (Archives gén. de méd., May, 1900).

Series of four cases of hemorrhage into the skin and suprarenal capsules, the interesting features of which were the sudden onset, rapid course and fatal termination. Not one of the patients was over a year old. The history throws absolutely no light on the causation of the disease; neither does the question of food appear to bear any relation to it. The presence of hemorrhage in the skin and suprarenal capsules would seem to make it more probable that the disease is some form of toxemia. In two cases the blood from the un-

opened heart was examined bacteriologically with negative results. In its extremely rapid and fatal termination the disease somewhat resembled the epidemic diarrhea and vomiting of infants. The general condition of the patients was different. They did not present the sunken eyes and the inelastic skin which is frequently met with in the epidemic diarrhea, and the cyanosis present in these cases is very rarely, if ever, seen in the skin and suprarenal capsules; the fact that Peyer's patches were much swollen is interesting. The authors believe that these symptoms are the manifestations of a special disease, and that the cause of this disease is a blood poisoning of some form, at present unknown. P. S. Blaker and B. E. G. Bailey (Brit. Med. Jour., July 13, 1901).

Three cases of sudden death in infants, due to hemorrhage into the suprarenal capsules. The train of symptoms is very definite. A child, previously well, is suddenly seized with acute abdominal pain and vomiting, the temperature rises, and one of the exanthemata is suspected. No characteristic rash appears, however, though sometimes there is purpura. Convulsions supervene, the patient becomes moribund, and death occurs in a few hours. If the condition is in infection presumably, it is a special infection of unknown origin. Bacteriological examination has proved negative in almost every case. Langmead (Lancet, May 28, 1904).

The writer was in attendance at birth of a full-term male child born after a normal labor. The umbilical cord, a thick one, was tied three times in succession on account of bleeding at the seat of ligation. This was finally checked and the child did well till the ninth day, when it became weak and jaundiced. In a few days more red patches appeared on the chin and later on various bodily areas. Fever and slight convulsions came on, and the child died on the twentieth day. Autopsy revealed a dark, slate-colored left adrenal. Opened *in situ,* it collapsed at once and emptied its fluid contents into the abdomen. On examination it appeared to be converted into a blood-sac, was very soft, and partly torn in removal. There were no signs of inflammation spreading up from the umbilicus, and the umbilical cord inside the abdomen was small, pale, and evidently not diseased. The brain was not examined.

The microscopic report was as follows: The right suprarenal showed no abnormal appearances. The left suprarenal was much broken up, but there were the remains of hemorrhage in its medullary substance, both in the form of extravasated corpuscles and as granules of pigment. B. G. Morrison (Lancet, June 6, 1908).

Case of a man 35 years old who succumbed in five days to adrenal hemorrhage. The disturbance was sudden in its onset, with symptoms resembling those of intestinal obstruction: violent abdominal pains, which morphine was powerless to relieve, continued vomiting, and absolute retention of gas and feces. Laparotomy was performed and showed the intestinal tract, including the appendix, to be entirely normal. The pain was in no way modified by operation. The temperature rose to 39° C. (102.2° F.), the pulse became extremely feeble, the respiration slow and shallow, and death took place on the fourth day after operation. The autopsy showed bilateral lesions of the adrenals, without other dangers of any kind. The left adrenal gave evidence of a recent and of a former hemorrhage (the patient had experienced a similar, though less severe, attack a few years before).

The condition of the abdomen, slowing of the pulse, with temperature remaining normal, should draw the attention from the intestinal tract to the adrenals. The case also indicates that this syndrome may not be fatal, and, if not fatal, may recur. Brodnitz (Münch. med. Woch., July 26, 1910).

In adults, most frequently subjects between 20 and 30 years of age, the attack may also be sudden, or preceded by

a period of great lassitude or asthenia. In most instances, however, the symptoms are such as to suggest acute intoxication or infection, with very severe pain, either in the epigastrium, the abdomen or below the costal margin, as the pre-eminent symptom. Then follow, in rapid succession, incoercible vomiting and, perhaps, diarrhea, and the signs of adrenal hemorrhage: great weakness of the pulse and rapid decline of the blood-pressure, hypothermia, cold sweats, coldness of the extremities, coma and death. This, may, however, be preceded by a typhoid-like state, delirium, convulsions and various perversions of the cutaneous pigmentation, varying from yellow to light-brown. In a series of 79 cases collected by Arnaud (1900) death occurred within a period ranging from a few hours to three days. The hemorrhage may be due to the rupture of a hemorrhagic cyst of the adrenals (treated under the next heading) and be preceded, therefore, by the symptoms peculiar to this condition.

The types of acute insufficiency of the suprarenals are classed by the writer as follows: (1) those of sudden onset; (2) the asthenic type; (3) the nervous type; (4) sudden death where nothing but a destructive lesion is found; and (5) cases which occur in hemorrhagic diseases. These types often overlap each other. In the asthenic type there is only extreme asthenia, followed in a few days by death. The nervous type includes those showing *convulsions, coma, delirium,* or *typhoid* states. In instances of convulsions the convulsion might well be the cause of the adrenal lesion. The first type is of particular interest because of its striking similarity to acute pancreatitis. The onset is sudden, "with *epigastric pain and tenderness,* vomiting, extreme prostration, feebleness and rapidity of pulse, coldness of extremities, lumbar tenderness, and, at times, diarrhea and abdominal distention, followed within a few days by death." The shock is more profound, the lumbar tenderness more acute, and the epigastric pain and vomiting less pronounced in adrenalitis than is usually the case in acute hemorrhagic pancreatitis.

Attention should be paid to the relative frequency of the condition in the purpuras of childhood and during or shortly after the acute infections; and due consideration must be paid to the apparent insufficiency and inflammations in the neighborhood of the suprarenals, s ırface burns, chronic heart or pulmonary disease, and any phenomenon tending to a great increase in internal blood-pressure. Lavenson (Archives of Intern. Med., Aug. 15, 1908).

ETIOLOGY.—That we are dealing with a relatively common morbid process is shown by the fact that Mattei, Rolleston and Le Conte, in 230 autopsies in the newborn, found adrenal hemorrhage in over 100 instances, or 45 per cent., while the proportion in adults is about 1 per cent. To explain the marked predilection of infants to this disorder many theories have been advanced: Weakness of the intra-adrenal vessels, either congenital or due to general disorders, such as syphilis, scorbutus, or, again, to lesions of the vascular walls, such as fatty degeneration, aneurism, etc.; lack of firmness of the medullary portion of the organ, the usual seat of the hemorrhage; compression by the uterus during labor of the inferior vena cava, thus offering resistance to the blood-streams from the adrenals which enter this great venous channel; ligation or prolapse of the funis, and other mechanical factors capable of causing passive congestion of all organs, including the friable and extremely vascular adrenals.

Case in a boy, aged 18, following operation for a left inguinal hernia,

though before the patient had been in perfect health. On the first day, January 28th, after the operation the pulse ranged from 100 to 140; it was normal on the second day, but from the third day, January 30th, until February 10th, it ranged from 100 to 140; after February 10th it was normal in rate but irregular until death, February 15th. The pulse was feeble all this time. The temperature was normal until the third day after the operation, when it gradually rose to 102° F., where it remained for two days, gradually going down to normal during the next five days. The day before death the temperature was subnormal. The urine at no time showed anything abnormal. Immediately after the operation the patient complained of pain a little to the left of the median line under the costal margin and later of the same kind of a pain under the right costal margin. This pain persisted with some tenderness until death. On the fifth day the liver reached three fingers below the costal margin and was then quite tender, but on the ninth day it seemed to have returned to its normal size; the tenderness, however, persisted. Some food was taken every day and there were no disturbances of the bowels, but the patient vomited at different times after the fifth day, gradually losing weight. The wound healed by primary intention. On February 9th the mind seemed somewhat clouded and gradually became more so until death occurred, February 15th.

Both suprarenal bodies were much larger than normal, firmly adherent to the surrounding structures, and densely and uniformly infiltrated with blood so that their appearance was like that of a hemorrhagic infarct. In places there was some infiltration of blood into the tissues about the suprarenal, but the main hemorrhage was wholly within this organ. On the cut surface it was quite smooth and red. The hemorrhagic infiltration was most intense in the medullary part and appeared to be of about the same age everywhere, and microscopically the tissue was uniformly necrotic, no nuclei being demonstrable in the adrenal cells; some of the vessels in the central part were plugged with clots and the mouth of the suprarenal vein was closed by a firm, adherent and yellow thrombus which projected into the vena cava as a small, smooth, oblong body about 1 cm. in the longest dimension. L. Hektoen (Jour. Amer. Med. Assoc., June 12, 1909).

Series of 124 infants in whom death occurred within eight days of birth. In 8 of these cases the necropsy revealed macroscopic hemorrhages in one or other adrenals. Two of these 8 cases were delivered spontaneously, 3 by version, 2 were foot presentations, and 1 was delivered by Cesarean section. The labors in most of the cases were difficult. Three had asphyxia, and the Schultze method of swinging was employed. In all but 2 cases the infants died within eight hours of birth. The autopsy in these cases showed usually anemia and icterus, and in every case hemorrhage with free bleeding in one or both adrenals. George Magnus (Berl. klin. Woch., Bd. xlviii, S. 1119, 1911).

While all these agencies probably cause hemorrhage in a certain proportion of cases, the majority are due, as stated above, to some form of intoxication, either toxins or endotoxins of infectious origin, or autogenous poisons, such as toxic waste products or autotoxins of intestinal origin. Some observers have ascribed the morbid process to a single hypothetical organism, but it has been clearly shown that different germs could produce it, including the *Staphylococcus aureus* and *albus* (Riesman), the pneumococcus (Hamill and Dudgeon), the pneumobacillus of Friedländer (Litzenberg and White), and others. In adults it occurs also, as a rule, as a complication of various diseases, some of which, such as septicemia, erysipelas and tuberculosis, are clearly of bacterial origin. Epilepsy, on the other hand, illustrates the class of cases

in which adrenal hemorrhage may be caused by autogenous poisons. In the adult, as shown under the next heading, several of these morbid processes may give rise to hemorrhagic cysts, which may eventually rupture into the abdominal cavity.

[That a general toxemia is an active factor in adrenal hemorrhage has been demonstrated experimentally. Roger (Le bull. méd., Jan. 21, 1894) found that inoculation of the guinea-pig by a pure culture of the pneumobacillus of Friedländer is followed by abundant hemorrhage of the suprarenal capsules, the blood bursting through the great capsular vein and causing necrosis of the elements by mechanical compression. These hemorrhages do not occur in the rabbit. Langlois (Le bull. méd., Feb. 7, 1894) saw hemorrhages produced by the pyocyaneus bacillus. Pilliet (Le bull. méd., Feb. 7, 1894) has also observed such hemorrhage after intoxication by essence and nitrate of uranium. C. E. DE M. S.]

The adrenals are exceedingly vascular, and at times are subject to emporary passive engorgement. Another cause of hemorrhage is unquestionably bacterial invasion, and several hemorrhages of considerable size have been reported as due to this cause. The hemorrhage may be also due to toxemia from irritating chemical poisons. In animals who have been injected for experimental purposes, with sera or antitoxins, as, for example, that of diphtheria, severe congestions and, occasionally, hemorrhages have occurred. A. J. M'Cosh (Annals of Surg., June, 1907).

Instance in an epileptic who died during an attack of enteritis, and in whom the autopsy revealed recent extensive hemorrhage in both adrenals. This seems to be a rare cause of death in adults, though not so uncommon in children. The reported case is one of Arnaud's asthenic type, probably due to circulatory failure from sudden removal of the tonus, producing secretion of the suprarenals. J. F. Munson (Jour. Amer. Med. Assoc., July 6, 1907).

Case of adrenal hemorrhage and acute edema of the lungs in the course of convalescence from acute nephritis due to erysipelas. The patient, a woman of 35 years, died suddenly on the fourth day of the nephritis, which had been brought on by exposure to cold. The autopsy showed, besides the evidences of pulmonary edema and intense acute nephritis, great distention of the adrenals by hemorrhage into them, with complete destruction of the medullary substance. Loederich (Le bull. méd., July 8, 1908).

From an extensive experience in autopsy work in the newly born, the writer believes that hemorrhage into the suprarenals is very common, and that the evidence is sometimes microscopic instead of macroscopic. He has found some degree of hemorrhage in infections due to the streptococcus, staphylococcus, pneumococcus. *Bacillus pyocyaneus,* the colon bacillus and a micrococcus he was unable to classify. We may have infections with the pneumococcus without any evidence of pneumonia. S. M. Hamill (Jour. Amer. Med. Assoc., Dec. 5, 1908).

Hyperplasia of the adrenal is an almost constant lesion in arteriosclerosis associated with chronic interstitial nephritis and left-sided hypertrophy, and it occurs with almost equal frequency in arteriosclerosis with chronic nephritis of the parenchymatous type; it is also a frequent lesion of arteriosclerosis without nephritis and of nephritis without arteriosclerosis. Adrenal hyperplasia is, consequently, probably the result of some factor active in a period of life in which these affections are most frequent. The adrenal lesion consists of increase of connective tissue, round-cell infiltration, increase in the thickness of the vascular wall and hyperplasia of the adrenal cells proper. Pearce (Jour. of Exper. Med., Nov., 1908).

PATHOLOGY.—An important function of the adrenals is to destroy products of metabolism. This was first

shown by Abelous and Langlois, whose views have been confirmed by many observers. Subsequently this function was found to apply to bacterial toxins. The prevailing view as to the pathogenesis of adrenal apoplexy is that, as a result of the *active* congestion of the adrenals incident upon infection and excessive functional activity and the high blood-pressure resulting therefrom, or *passive* congestion due to factors which prevent the free passage of blood out of the organs, such as pressure upon the adrenal veins, the inferior vena cava, etc., the capillaries become engorged and yield, thus causing a more or less diffuse interstitial hemorrhage. In some instances the entire adrenal parenchyma is destroyed, and the organ is more or less dilated by the blood accumulated in it, and may thus form a brownish or reddish-blue mass, varying in size from that of a small walnut to that of the underlying kidney. In other cases the organ ruptures, the blood flowing into the peritoneum or the abdominal cavity. Both adrenals are involved in the morbid process in most instances. Other organs, the lungs, the pleura, and skin in particular, may also be the seat of hemorrhage, the purpura witnessed in a large proportion of cases being naught else than a punctiform hemorrhage into the cutaneous tissues, due to excessive vascular tension. Death may be due to these hemorrhages or to the annihilation of the functions of the adrenals.

> Small ecchymoses into the adrenals occur frequently in the various infectious diseases and are to be considered toxic in origin. Hemorrhagic infarction of both adrenals often leads to peritonitis and collapse and may result in death. It may, however, occur without any of these sequences. Large hematomata may be found in the adrenals. Hemorrhage into these glands may also occur under the following circumstances: traumatic influences (under this class is found the form seen in the newborn); hemorrhagic diathesis; thrombosis of the suprarenal veins, which is the most common cause; and bacterial capillary embolism, which occupies the second rank. The thrombi can affect the trunk or the tributaries of the suprarenal veins; they can occur in both or only in the right organ; they are to be regarded as marantic thrombi, occurring, as a rule, only in individuals suffering from some form of chronic disease. The peculiar anatomical disposition of the vessels favors their formation. A primary suprarenal disease does not precede these cases. Under the cases of bacterial capillary emboli are included those in which neither clinically nor anatomically can septic disease be observed. Bleeding into the adrenals may lead to atrophy of the organ. M. Simmonds (Virchow's Archiv, Nov. 3, 1902; Med. News, Dec. 27, 1902).

Acute hyperadrenia and adrenal hemorrhage in the infant may also be due to toxemia. While the fetus is *in utero* its waste products are transferred to the maternal blood and converted therein into eliminable products. When its birth occurs it is left to its own resources, and if it is unable fully to break down its waste products these accumulate in its blood. Its waste products—and this applies as well to certain toxins, including those enumerated above—excite powerfully both the adrenal system and the vasomotor center (hence the flushing following a copious meal). If the adrenal system can thus be made to prevail, the wastes (or toxins) will be gradually destroyed, and the vasomotor center will not be abnormally excited. If it is not, the wastes accumulate, and the vasomotor center being powerfully stimulated, the vascular tension and the blood-pressure become intense; this being further enhanced by the excess of adrenal

secretion produced, the pressure becomes such that the adrenal tissues, already overburdened with blood as a feature of their overactivity, yield—along with many cutaneous capillaries, as witnessed by the hemorrhagic purpura.

Case of a child who had been brought to the Bellevue Hospital with no further history than that it had been blue since birth. It had died very suddenly a few minutes after entering. At the autopsy, the abdominal cavity was found filled with blood, and the intestines all matted together by very firm adhesions. On the superior surface of the adrenals, represented by a more or less organized blood-clot of a considerable size, was an opening two inches in diameter, through which the blood had escaped into the abdominal cavity. On examining the foramen ovale it had been found nearly closed. The ductus arteriosus as it entered the aorta presented a funnel-shaped opening. Hematomata of the suprarenals are rarely as large as the one presented. This is the second case of the kind that the writer has met with. He has been able to find only one or two instances reported in the literature in which rupture had taken place into the peritoneal cavity. One observer reported 26 cases in which there have been small hemorrhages into the suprarenal in a series of over 100 autopsies on stillborn infants. In 2 of the cases the hemorrhage had started in the cortex. Charles Norris (Med. Record, June 9, 1900).

Examination of the adrenals in 16 cases of diphtheria, 10 of variola, 23 of lobar- and broncho- pneumonia, 5 of typhoid fever, 1 of tetanus and 4 of streptococcus infection. The glandular cells were profoundly altered. There was also hemorrhagic extravasation into the stroma, in which the polynuclear neutrophilic leucocytes are especially abundant. True abscess formation occurs chiefly in the prolonged infections of variola and typhoid fever. No peculiar alterations were observed as the result of special infections and the changes in general were common to all the cases examined. A pericapsular sclerosis, cortical and central, was present in most cases. This chronic lesion is not due to the acute process, but is to be regarded as the result of previous repeated or continued infections. The writers regard the adrenals as possessing an important function in the resistance of the organism to infection. Oppenheim and Loeper (Archives de méd. exper., Sept., 1901).

Case of a male infant, four days old, who was born after a normal labor. On the fourth day after birth the infant ceased to pass urine and after total suppression for twenty-four hours it died. At the autopsy the chief interest centered in the suprarenal bodies; the left one was replaced by a tumor the size of a hen's egg and the right one presented a tumor as large as a cherry at its apex. The structure of both tumors was identical, both showing a hypoplasia of the fascicular zone followed by marked fatty changes and necrosis. In the case of the growth in the left suprarenal body, liquefaction of the necrosed central portions gave rise to a cyst which was filled with cell *débris*. Both growths were considered to belong to the group of adenoma. A. S. Warthin (Archives of Pediatrics, Nov., 1901).

Results obtained by inoculating rabbits and guinea-pigs with cultures of various micro-organisms. The micro-organisms used were diplococci, typhoid bacilli, bacterium coli, *Staphylococcus aureus,* streptococci, anthrax bacilli, and diphtheritic bacilli. In the experiments with active cultures there was always great hyperemia of the suprarenal bodies and in the more active cases there were hemorrhages. E. Frederici (Lo Sperimentale, lviii, Fasc. 3, 1904).

Common pathological changes found in the suprarenals are hemorrhage, which converts the medulla of the organ into a pulpy mass, and embolism of the suprarenal artery, whereby the entire organ is destroyed. Occasionally, one or both organs will be converted into

the large bluish tumors, whose contents are fluid blood. This is especially common in the newly born, and many believe that the motions necessary for artificial respiration are the real cause. In a number of cases observed by the author, however, artificial respiration was not resorted to, and it is likely that severe labor, particularly if the child is in the breech position, will furnish the necessary trauma to rupture the friable suprarenal tissue and thus give rise to a hematoma. If both organs are affected the symptoms are those of Addison's disease, and death rapidly sets in. S. Oberndorfer (Wiener klin. therap. Woch., June 18, 1905).

It has been demonstrated that the adrenals have the function of neutralizing or destroying poisonous products resulting from muscular work; also those of uremic poisoning, and of poisons introduced from without. The author found as a result of experiments in rabbits, that they also neutralize the poisons circulating in the blood as a result of burns. In the case of animals dying within a few hours after the burns, he noted only a marked dilatation of the vessels of the suprarenal capsules; after a longer period a marked hyperemia resulted; after three to five days the capsule was increased in volume, and there was hyperplasia of the glandular epithelium, testifying to an increased activity of the organ and a proliferation of the cells. Augusto Moschini (Gaz. Med. Lombarda; Med. Record, March 25, 1905).

Conclusions based on a study of 119 cases including 2 personal cases: 1. Hemorrhage of the suprarenal capsules is more common than hemorrhage in the other viscera. 2. This is due primarily to the close relation of the adrenals to the vena cava, making congestion easy, and to the peculiar anatomical construction which favors hemorrhage. 3. A weakness of the vessel walls, either normal delicacy or pathological alteration favors the rupture. 4. The place of election of the hemorrhage is usually in the internal cortical zone because of its vascularity and the anatomical arrangement of the vessel. 5. The bleeding always follows active or passive congestion. 6. Passive congestion may be caused by difficult labors, obstetric operations, thrombosis, or, in short, anything that would favor venous stasis. 7. Active congestion is induced by infection or any toxemia which incites hyperemia by a superactivity of the gland. 8. The findings of the pneumobacillus of Friedländer in the 2 cases personally reported and other bacteria in 5 additional cases prove beyond question that infection is a cause of adrenal hemorrhage. 9. Death results either from loss of blood or an interference with the physiological function of the gland. J. C. Litzenberg and S. Marx White (Jour. Amer. Med. Assoc., Dec. 5, 1908).

TREATMENT.—The literature of the subject is suggestively silent on the prevention and treatment of this condition. The foregoing conception of its pathogenesis, however, opens a greater field in this connection.

As to prophylaxis, it must be borne in mind that acute hyperadrenia is present when the blood-pressure and the febrile process are abnormally high. Antipyretics are worse than useless, since they further increase the blood-pressure and through this fact the danger of adrenal congestion, which may lead to hemorrhages. The physiological **saline solution** offers, on the other hand, all desirable qualities. It does not, as argued theoretically by some authors, increase the vascular tension, even if injected intravenously, as shown by the experiments of Sollmann (Archiv f. exper. Path. u. Pharm., Bd. xlvi, S. i, 1901), Briggs (Johns Hopkins Hosp. Bull., Feb., 1903), and others, any excess of fluid leaves the vessels at once. By reducing the viscidity of the blood, saline solution tends to relax the blood-vessels; by increasing its osmotic properties it facilitates greatly the penetration of the plasma into the lymphatic chan-

nels, thus further reducing the vascular tension. The bactericidal and antitoxic properties of the blood are not reduced in the least by this procedure; there is considerable evidence available to show, in fact, that they are enhanced (see "Internal Secretions," 4th ed., vol. ii, p. 1367, 1911). Saline solution, therefore, should be used intravenously in emergency cases; subcutaneously in threatening cases, and per rectum in all cases in which there is any likelihood whatever that adrenal hemorrhage might occur. If employed from the *onset* of all infections, as I suggested in 1903, the blood-pressure would probably never be raised sufficiently to endanger the adrenals.

As to drugs, we have several at our disposal which lower the blood-pressure. In emergency cases **nitrite of amyl** by inhalation, with **nitroglycerin** (or, in children, the **sweet spirit of niter**) to sustain the effect, appears indicated. **Chloral hydrate** has been used advantageously by J. C. Wilson in certain exanthemata, to subdue the cutaneous discomfort and as a sedative; as it is also a vasomotor depressor, it might also serve advantageously in all but infants in whom the respiratory mechanism is defective. **Veratrum viride** suggests itself as another useful agent of this class. Of all measures, however, the saline solution is much to be preferred.

When the hemorrhage has occurred the lethal phenomena are of such short duration in most cases as to have suggested, we have seen, the term "adrenal apoplexy." In a fair proportion of cases, however, the hemorrhage causes sudden hypoadrenia. The treatment of this condition is that indicated in the emergency cases of terminal hypoadrenia (see page 441). If the hemorrhage has not been too extensive the chances of recovery will be greatly increased by the use of **adrenal** or **pituitary preparations**, the latter owing its properties, in my opinion, to the adrenal chromaffin substance the pituitary contains. These agents will help to sustain oxidation and metabolism while the adrenal lesion is undergoing resolution.

HEMORRHAGIC PSEUDOCYSTS OF THE ADRENALS.—In most instances hemorrhagic blood-cysts are the results of acute hyperadrenia in the course of some infection or intoxication in which the adrenal hemorrhage has been limited to a small area, which eventually develops into such a cyst.

SYMPTOMS.—These growths may give rise to no symptom, other, perhaps, than a sensation of weight, until quite large, when pain supervenes. This is at first indefinite, though most marked in the region of the tumor, in the right or left loin, or in the upper portion of the abdomen and loin. The neuralgia-like pain becomes increasingly severe, and radiates in various directions, especially toward the hip and thigh of the corresponding side, and is subject to exacerbations, which may be very severe, especially after meals. Epigastric pain and vomiting—which affords relief—occur in some cases, especially during these exacerbations of suffering.

The tumor may manifest itself at first merely by enlargement of the abdomen. The bulging then becomes more clearly defined on one side or the other (this variety of growth being almost invariably unilateral), under the lower ribs, which may be pushed outward if the growth is sufficiently large, or below their free border, *i.e.*, between them and the superior spine of the ilium. If the tumor, which grows downward and forward, is sufficiently below the ribs to be palpated, it is usually found globular, or

oval, smooth and tense, though elastic, to the touch. Fluctuation may also be elicited. In some cases it is immovable under palpation, though it may, at first, follow the respiratory movements. Nor can it be grasped as is sometimes possible in renal tumors; if small, the tumor is movable, either upward or downward, but this mobility gradually decreases as the tumor develops. The growth is sometimes sensitive under pressure.

At first, several years, perhaps, the patient may appear normal in every other respect, be well nourished, ruddy, etc. With comparative suddenness, however, he begins to fail, losing flesh rapidly, all the other symptoms mentioned, to which dyspnea and a sense of constriction about the chest is added, becoming more severe. If the cyst does not rupture, polyuria, hematuria, and even slight bronzing may appear. It is probable, however, that this train of phenomena is witnessed only in a very small proportion of cases, rupture and hemorrhage constituting the "adrenal hemorrhage" in adults treated under the preceding heading, being the outcome in practically every instance.

> Adrenal hemorrhage in the newborn is probably not uncommon, but in the great majority of cases there are no symptoms to indicate the occurrence of such a lesion, and the hematoma is quickly absorbed. It is equally difficult to understand why in adults these hemorrhages should occur. The deep situation of the adrenal bodies would seem to be sufficient protection from injury, except that of the severest character, and yet in a certain proportion of these cases the cause has aparently been a trauma. A. J. M'Cosh (Annals of Surg., June, 1907).

[This abstract indicates the drift of the prevailing conception of the pathogenesis of these growths. While local lesions are ascribed to the concomitant disorder, the adrenals, being supposedly affected directly by the toxin or poison that may be present, are thought to explain some cases, others require, it is believed, some form of traumatism. It is to the *excessive blood-pressure produced by the toxin* that the vascular ruptures to which the hemorrhage is due should be ascribed. C. E. DE M. S.]

DIAGNOSIS.—The symptomatology of adrenal cyst, apart from the location of the tumor, does not present, as just shown, very characteristic features. The location of the pain sometimes suggests *intercostal neuralgia;* but inasmuch as pain occurs only when the growth is large, percussion and palpation will reveal the presence of a tumor. In neuralgia the pain is also apt to be localized, thus distinguishing it from the radiating pain of adrenal cyst. The sudden onset of severe pain may be taken for *acute pancreatitis.* The location of pain and tenderness in the upper left abdominal quadrant, the subnormal temperature and the early lethal trend—death occurring sometimes within three days—clearly point to the latter disease. *Pancreatic cyst* is also differentiated by its location and its association with glycosuria, stearrhea, and imperfect digestion of fats and albuminoids. *Hydatid cyst of the liver,* another source of confusion, is attended by the presence of biliary pigments in the urine, the appearance of cysts in the stools and vomited matter, and with obstruction phenomena. *Cancer of the spleen* may be recognized by the more nodular outline of the growth and the cachectic phenomena.

Hydatid cyst of the spleen is usually associated with hydatid cysts elsewhere, and may be accompanied by the presence of hooklets in the excretions. Puncture of the growth should be carefully avoided when there is any suspicion whatever that an adrenal blood-cyst is present. *Renal cysts* are

more easily palpated bimanually, and are usually freely movable.

> Only nine cases of large serous cysts of the adrenals are on record. Case personally observed, in which a serous cyst, probably of lymphatic origin, had developed in the left suprarenal capsule. As the other suprarenal was sound, there were no signs of Addison's disease. Tumors of this kind have a very slow development, but gradually push up the diaphragm, distending the lower part of the thoracic cavity and finally protruding in front below the costal arch. The neighboring organs are displaced to a remarkable extent, and compression of the abdominal sympathetic is liable to cause severe pains. Terrier and Lecène (Revue de Chir., vol. xxvi, No. 9, 1906).

ETIOLOGY.—Adrenal blood-cyst has been ascribed to many morbid conditions. Acute intoxications, especially diphtheria, typhoid fever, burns, osteomyelitis, hepatic abscess and tuberculosis, have been regarded as initial factors of these growths, a small cyst formed during the active stages of these diseases, or, as a complication thereof, gradually increasing in size until the foregoing phenomena or adrenal hemorrhage occur. In the light of the data submitted in the foregoing pages, they are merely after-effects or complications, in other words, of the damage done to the adrenals during an acute febrile toxemia.

Atheroma of the adrenal arteries is also regarded, and doubtless justly, as a source of initial lesions, but it is probable that cerebral lesions of the same kind and apoplexy, which have been considered by some authors as etiological factors, are merely concomitant lesions due to general arteriosclerosis. Thrombosis of the adrenal vein by blocking the efferent circulation has also been incriminated, while traumatism is known to have started the morbid process in at least two instances.

PATHOLOGY.—While older investigators, including Klebs, Virchow and Heuschen, considered these growths as retention cysts, similar to those formed in the thyroid, and thus termed them "struma adrenalis," the prevailing view at the present time is that a small hematoma or an acute congestive process—though erroneously, in my opinion, ascribed to *local* intoxication—initiates the growth. As the latter increases in size the adrenal structure is gradually destroyed and the content is no longer—unless a recent hemorrhage has occurred—merely blood, but a more or less fluid magma of detritus, broken-down blood- and tissue- cells, flakes or fibrin, cholesterin crystals, etc., which may be dirty yellow, greenish or brownish in color. Microscopically, the walls of the cyst, which vary from $\frac{1}{16}$ to $\frac{1}{8}$ inch in thickness, are composed of fibrin tissue; the inner aspect shows shreds or remnants of the adrenal cortex.

Certain thickened portions of the capsule and what semiorganized clots the cyst may contain may be found to include small cysts, chalky deposits. These growths sometimes become very large—as large as an adult head in a case of Chiari's—and contain several pints of blood or liquefied blood and tissue elements.

PROGNOSIS.—The fact that this growth is practically always unilateral, and that the loss of one adrenal does not compromise life, as does removal of both organs, make it possible to remove the growth with safety. The frequent instances of severe collapse and shock that have followed these operations suggest that the operative prognosis can-

not but be improved by resorting to those surgical procedures which will entail the least possible handling of the intraperitoneal organs and of the sympathetic ganglia, all of which are well known to produce shock readily by reflex action.

TREATMENT.—The treatment is, of course, entirely surgical. The cyst may be removed through either an abdominal or lumbar incision. In accord with M'Cosh's advice, which a review of the operative results recorded fully sustains, preference should be given to the **lumbar incision.** The approach is more direct; it avoids the handling of the intraperitoneal organs, which must necessarily take place if the tumor be reached through the abdominal incision, and it affords the most direct route for drainage. In the average case, an oblique incision from behind downward and forward below the last rib, which has been found most convenient for extirpation of the kidney and ureter, is as applicable here. If much space is needed, it is safer to remove the last rib than, as some European surgeons have advised, to resort to the abdominal incision, which, as previously stated, entails considerable shock. The tumor is sometimes found so firmly adherent to the kidney that removal of this organ becomes necessary.

Personal case in which the growth was successfully removed through a **lumbar incision.** The main dangers of the operation are hemorrhage from the pancreas or the larger veins, and injury to the descending colon or to the sympathetic plexus. These cysts are usually very adherent and considerable time is consumed, and blood lost in enucleation of the sac. The adhesions toward the vertebral column and abdominal aorta are especially troublesome, and in some of the cases subjected to operation have prevented complete removal of the cyst. Severe collapse has followed many of the operations. This may be due to blood lost, time of exposure, shock due to peeling the tumor from the diaphragm or sympathetic nerves. A. J. M'Cosh (Annals of Surg., June, 1907).

In the case of large serous cysts complete **extirpation** should be practised if possible; but if the sac cannot be readily and gently detached from the surrounding parts, the surgeon should rest content with partial resection of the wall of the cyst, and with the method of marsupialization, in which the margins of the sac are attached to the external wound and the cavity is packed and drained. The results of the operative treatment of large suprarenal cyst have not, up to the present time, been satisfactory. Five cases only have been thus dealt with, of which three were fatal. Terrier and Lecène (Revue de Chir., vol. xxvi, No. 9, 1906).

FUNCTIONAL HYPOADRENIA.

DEFINITION.—Functional hypoadrenia is the symptom complex of deficient activity of the adrenals, due to inadequate development, exhaustion by fatigue, senile degeneration, or any other factor which, without provoking organic lesions in the organs or their nerve-paths, is capable of reducing their secretory activity. Asthenia, sensitiveness to cold, and cold extremities, hypotension, weak cardiac action and pulse, anorexia, anemia, slow metabolism, constipation, and psychasthenia are the main symptoms of this condition.

SYMPTOMATOLOGY AND PATHOGENESIS.—The process of development in the child and the influence of senility on the adrenals make it necessary to discriminate between the main stages of life, infancy, childhood, adult and old age, in describing this condition.

Infancy.—Although the adrenals are relatively large in the infant (one-

third the size of the kidney at birth), their functions are limited to the carrying on of the vital process, at least during the first year of life, the mother's milk supplying the antitoxic products capable of protecting it against the destructive action of poisons of endogenous and exogenous origin. This protective influence of maternal milk is clearly defined in the following quotation from Professor William Welch's Harvey Lecture: "It is an important function of the mother to transfer to the suckling, through her milk, immunizing bodies, and the infant's stomach has the capacity, which is afterward lost, of absorbing these substances in active state. The relative richness of the suckling's blood in protective antibodies, as contrasted with the artificially fed infant, explains the greater freedom of the former from infectious diseases." Striking proof of this is afforded by the fact that during the siege of Paris, in 1870-71, according to J. E. Winters ("Practical Infant Feeding," p. 6), "while the general mortality was doubled, that of infants was lowered 40 per cent. owing to mothers being driven to suckle their infants."

Childhood.—The predilection of children to certain infectious diseases obviously indicates that it is not only in infancy that vulnerability to these disorders exists; it exposes life during the first decade, and more, of the child's existence. If, then, in the infant the maternal milk, as Welch says, protects the suckling against such diseases, at least to a considerable extent, we must conclude that the same underlying cause of vulnerability persists several years, *i.e.*, until it has in some way been overcome. The adrenals acquire, with other organs, the power to supplant the mother in contributing antitoxic bodies to the blood; they supply internal secretions which fulfill this rôle.

These facts point to the adrenals as at least prominent organs among those whose inadequate development explain the special vulnerability of children to certain infections, the "children's diseases." It becomes a question now whether there are degrees of this hypoadrenia which render the child more or less liable to infection.

That degrees of hypoadrenia exist in children is, in reality, a familiar fact to every physician when the signs of this condition are placed before him. The ruddy, warm, hard-muscled, heavy, out-of-door, romping child with keen appetite and normal functions, is one in whom the adrenals are as active as the development commensurate with its age will permit. He is ruddy and warm because oxidation and metabolism are perfect and the blood-pressure sufficiently high to keep the peripheral tissues well filled with blood; his muscles, skeletal, cardiac and vascular, are strong because, in addition to being well nourished, they are exercised and well supplied with the adrenal secretion, which, as shown by Oliver and Schäfer, sustains muscular tone. As normal outcome of this state, we have constant stimulation of the functional activity of the adrenals. The muscular exercise and maximum food-intake involve a demand for increased metabolism and oxidation, and the resulting greater output of wastes imposes upon the adrenals, as participants in the oxidation and autoprotective processes, greater work, more active growth and development, with *increase of defensive efficiency* as normal result.

The pale, emaciated, or pasty child, with cold hands and feet, flabby muscles, whose appetite is capricious or deficient—the pampered house-plant so

often met among the rich—represents the converse of the healthful child described, just as does the ill-fed, perhaps overworked, child of the slums. The emaciation, the cold extremities, indicate deficient oxidation, metabolism and nutrition owing to the torpor of the adrenal functions; the pallor is mainly due to a deficiency of the adrenal principle in the blood and to the resulting low blood-pressure, which entails retrocession of the blood from the surface. This child is not ill, but the hypoadrenia which prevails normally, owing to the undeveloped state of its adrenals, is abnormally low, and it is vulnerable to infection.

That all conditions which in the adult tend to produce functional hypoadrenia affect the child at least to the same extent, is self-evident.

Adult Age.—As in the child, the adrenals may be inherently weak. Such subjects do not, as in hypothyroidia, show signs of myxedema; but their circulation and heart action are feeble, they tend to adiposis, and show other signs of hypoadrenia. I have witnessed suggestive bronze spots in such cases. As a rule, however, the development of the adrenals in adults is an accomplished fact—as also that of their coworkers in the immunizing process, the thyroid and pituitary, we shall see. The adrenals, fully capable of sustaining oxidation and metabolism, are able to defend the organism adequately; indeed, they do more: by sustaining oxidation and metabolism up to its highest standard in all organs, they also preserve the efficiency of all other defensive resources, including phagocytosis, with which the body is endowed to their highest level. On the whole, the *normal adult whose adrenals functionate normally is relatively resistant to infection.* The infrequency with which we are infected, notwithstanding daily exposure in our professional work, attests to this fact.

Functional hypoadrenia appears, however, when, irrespective of any disease, and as a result of the vicissitudes of our existence, the adrenals are subjected to abnormal secretory activity.

Fatigue is a prominent factor in this connection. Mosso's ergograph shows clearly the functional efficiency of the forearm. If by means of this instrument we compare the muscular power of a case of Addison's disease with that of any other kind of sufferer, whose muscles are organically normal, a striking difference will be noticed: signs of fatigue appear very soon, and muscular impotence asserts itself where an advanced case of tuberculosis, for example, will be able to show appreciable strength. Intense asthenia is, in fact, a symptom of Addison's disease almost as characteristic as the bronze spots. It is as pre-eminent after experimental removal of both adrenals. This harmonizes with Oliver and Schäfer's demonstration of the influence of the adrenal secretion over muscular tone. Many other proofs could be adduced to show that there is a close relationship between fatigue and the functions of the adrenals. The pale and drawn face of an exhausted man, the readiness with which he suffers from the effects of cold and exposure, especially in the intestines, are familiar features of daily life.

The unusual prevalence of disease among soldiers in the field is, of course, partly due to the defective sanitation that a campaign entails; but fatigue—particularly that due to heavy marching, carrying heavy accoutrements—is, in my opinion, an important predisposing cause, through its influence upon the adrenals. Not only are these organs

called upon to sustain general oxidation and metabolism at a rate exceeding by far that which amply suffices for normal avocations, but the fact that, as shown by Abelous and Langlois (*loc. cit.*), they also serve to destroy the toxic products of muscular activity, constitute another cause of drain upon their secretory resources. "Fatigue," write Morat and Doyon (Traité de Physiologie," Art. "Secretions Internes," p. 441, 1904), referring to experimental fatigue in animals deprived of their adrenals, "has an aggravating influence, as first indicated by Abelous and Langlois, and confirmed by Albanese and all authors. Hultgren and Andersson have even observed sudden death as a result of powerful movements of the body."

Debility from any source, starvation, loss of blood, etc., as efficiently renders the body vulnerable to disease: "Combine toxin and antitoxin, and inject the mixture," writes Professor Charrin ("Les Défenses Naturelles de l'Organisme," p. 63, Paris, 1898); "no harm will follow. But weaken the animal by starvation or slight bleeding and administer the same injection; death will follow with all the signs of poisoning by the toxin, with congested adrenals." , , , "That relations exist between the adrenals and infection," urges the same authority, "is today an incontrovertible fact." It follows, therefore, that hypoadrenia from any source should render the body vulnerable to disease. Deficient food, excessive work, that of the sweat-shops for example, account for much of the predilection of our slums as foci of disease, their filth nurturing the appropriate germs.

Masturbation and excessive venery are important morbid factors in this connection. The pallor and asthenia witnessed in these cases, so far unexplained, can readily be accounted for if, as I believe, the liquid portion of the semen is rich in adrenal principle. This is suggested by the fact that spermin, the purest of testicular preparations, gives the same tests and acts precisely as does the adrenal principle. The latter is an oxidizing body acting cata lytically; it resists all temperatures up to and even boiling; it is insoluble in ether and practically insoluble in absolute alcohol, and gives the guaiac, Florence, and other hemin tests. Now, spermin not only raises the blood-pressure, slows the heart and produces all other physiological effects peculiar to the adrenal principles, but its solubilities are the same; it gives the same tests; it resists boiling. Moreover, it is regarded in Europe as a powerful "oxidizing tonic," and has been found equally useful in disorders in which adrenal preparations had given good results. The inference that spermin consists mainly of the adrenal product suggests that it should not be regarded as specific to the testes, but, instead, a constituent of the blood at large; not only did this prove to be the case, but it was found in the blood of females as well as in that of males.

Old Age.—Perpetual life would doubtless be ours were it not that all living organic matter is subjected, after more or less precarious periods of growth and adult existence, to one of decline and final disintegration. This applies particularly to the adrenals, if their functions are, as I hold, to sustain oxidation and metabolism, the fundamental processes of the living state. Indeed, the senile state may be said to be as evident in these organs as it is in the features of the aged.

Series of corrosion preparations, of the veins of the left adrenal in different

people, aged, respectively, 22, 30, 80, and 82, using the same injecting substance and technique. They showed conclusively that the vascular system of the adrenals becomes steadily smaller as adult age wanes, being greatly shrunken in old people. Landau (St. Petersb. med. Woch., June 14, 1908).

According to Landau (St. Petersb. med. Woch., June 14, 1908), Ecker, Henie, and von Kölliker found that fat occurred in increasing quantities in the adrenal cortex as age advanced, while Hultgren and Andersson found fibrous tissue between the cortex and medulla in very old animals. Minervini (Jour. d'anat. et de physiol., pp. 449 and 639, 1904) found a similar condition in the medulla of aged individuals. Dostojewski, moreover, observed a marked—occasionally very great—reduction in the size of the adrenals in the aged. Rolleston (Lancet, Mar. 23, 1895) has also called attention to this fact.

Landau studied the influence of age on the vessels, large and small, of the adrenals, adopting for the purpose a process introduced by Rauber and applied by many others, including Bezold, Hyrtl, and Lieberkühn, to the study of other organs, viz., injection of the vessels with some hardening substance, and the subsequent use of a corrosion method to destroy the parenchyma. The adrenals receiving their blood through a number of small arteries, the adrenal vein, which contains no valves, was used for the injection. The annexed plate shows the result. The vessels, and therefore the adrenals, are well developed and in full bloom, as it were, in the adrenals of the three young adults, while those of the aged are shrunken and correspondingly deficient as blood-channels—a certain index of the lowered activity of the adrenal functions, and, through these, of the vital process they sustain.

The asthenia of old age thus finds a normal explanation in the defective supply of adrenal secretion—precisely as it does in Addison's disease. In fact, Rolleston states that atrophy of the glands in the young may produce this disease. Lorand ("Old Age Deferred," Am. ed., p. 111, 1910), in his recently published book on old age, urges, in fact, that "old age is caused by degeneration of the ductless glands, and that there exists a condition of autointoxication in old age" quite in keeping, I may add, with a decline of the antitoxic power shown by the adrenals. Lorand, who has antedated others in showing the influence of the ductless glands upon old age, has found his views confiremed by Campbell (Lancet, July, 1905), Pineles, Sir Herman Weber, and also—though he denies a relationship between old age and myxedema—Metcnnikoff.

In his closing remarks on the causation of old age, Lorand remarks: "It is evident from the above considerations that all hygienic errors, be they errors of diet or any kind of excess, will bring about their own punishment, and that premature old age, or a shortened life, will be the result. In fact, it is mainly our fault if we become senile at 60 or 70, and die before 90 or 100." Hence the motto of his title page:—

"Man does not die,
He kills himself."
—*Seneca.*

In the light of the data I have submitted, however, it is clear that the lesions to which the adrenals are subjected during infections and autointoxication, from birth to the last day of life, do greatly shorten it by limiting the functional area of the organs through the local fibrosis they entail. It is quite

probable, in fact, that centenarians owe their prolonged longevity mainly to integrity of their adrenals.

Hygiene, and particularly those of its divisions which bear directly upon the prevention of infectious diseases, thus asserts itself as one of the most useful of our sciences in another direction, viz., that of preserving the organism against those diseases which, seemingly benign because they are recovered from, measles for example, in the end shorten our existence by compromising the integrity of the organs which sustain the vital process itself.

Prophylaxis and Treatment.— Though we are dealing with depraved states of a physiological condition, we cannot but regard them as abnormal in the sense that we deem adynamia abnormal, and, therefore, susceptible to remedial measures. Indeed, there is much that can be done in each of the three forms of functional hypoadrenia described.

In the **infant** we should, by every possible means, prevent infection or intoxication to preserve the integrity of their adrenals and other autoprotective organs. The key of the whole situation lies in the fact that, as Ruhräh states, "nearly all the cases and nearly all the deaths are in bottle-fed babies." Physicians are, as a rule, entirely too ready to yield to the demands of social and other claims put forth by mothers who do not wish to nurse their offsprings. The responsibility assumed by both mother and physician under these circumstances is overlooked. I cannot but hope that if this continues, and the sacrifice of countless infants proceeds, laws may be enacted to prevent it by imposing upon the physician the duty of submitting to the State authorities a certificate in which sound reasons shall alone account for his consent to a departure from nature's methods which entails deaths untold. J. Lewis Smith states that the death rate among foundlings in New York City reached almost 100 per cent. until wet-nurses were provided. Men such as Jacobi, Winters, and many French authorities have written forcibly upon this subject, but seemingly to no avail. The holocaust continues.

Experimental research in the same direction has only served to emphasize the all-important prophylactic value of **maternal milk.** As L. T. de M. Sajous (Univ. of Penna. Med. Bull., June, 1909) states: "That milk is capable of conveying antitoxic substances after these have been injected into the mother has been known for a number of years. In 1892 Ehrlich and Brieger demonstrated this fact in their experiments on mice. The offspring of non-immune mice were suckled by other mice which had been immunized against the actions of certain poisons. It was found that the young were thereby rendered immune to the poisons employed, viz., ricin, abrin, and tetanus toxin. This immunity steadily increased during the period of lactation, persisted for some time after, and then gradually disappeared. Ehrlich thus showed that a passive immunity was created in the young by the absorption of milk from an immune adult, and even went so far as to assert that all so-called heredity immunity was, in reality, of the passive variety, being transmitted during lactation and not inherent in the offspring itself.

"This transmitted immunity has been shown to occur in various other animals. Thus, in 1893, Popoff showed that immunity against cholera could be transmitted through cows' milk. He injected bouillon cultures into the peritoneal cav-

ity of a cow, and later injected into guinea-pigs from 2 to 10 c.c. of the cow's milk. The guinea-pigs become immune against cholera. The same observer noted also that, when the milk was boiled before injecting it, no immunity was produced. Kraus showed that the milk of goats immunized by injections of 'typhus-coli bacilli' and cholera organisms had protective and agglutinating properties. He also ascertained that the relative proportion of agglutinating substance present in milk to that contained in the serum was as 1 to 10. Taking up the subject from the standpoint of tuberculosis, Figari showed, in 1905, that the agglutinins and antitoxins of this disease appeared in the milk of cows and goats that had been actively immunized against it. In another series of experiments he fed the milk of immune cows to a number of rabbits, and in others injected it subcutaneously. In both cases these animals, thus passively immunized, were found to transmit to their young, by their milk, the agglutinins and antitoxins of tuberculosis.

"Evidence is not lacking of the transmission of antitoxic substances through human milk. It has long been known that infants below one year of age were but slightly susceptible to certain infectious diseases, and in particular scarlet fever, diphtheria, measles, and mumps. In fact, it was an attempt to throw some light on this subject that Ehrlich performed his classic experiments on mice in 1892. Four years later Schmid and Pflanz performed some interesting experiments on guinea-pigs. Into some of the animals they injected blood-serum derived from human blood which was taken, at the time of delivery of her child, from a woman to whom had been administered diphtheria antitoxin. Into other guinea-pigs they injected milk from the same woman. The animals were then given injections of the ordinarily fatal dose of diphtheria toxin. From the results obtained the investigators concluded (1) that antitoxin substances found in the blood of parturient women exist also in the milk; (2) that the quantity of antitoxic substances excreted with the milk is much less than that found in the blood. Similarly, in 1905, la Torre injected diphtheria antitoxin in several wet-nurses, and noted the antitoxic power resulting in the blood of the nurslings by injecting measured amounts of this blood mixed with diphtheria toxin into guinea-pigs. He was able to satisfy himself that a passage of the antibodies occurred in small amounts into the blood of the infants.

"These experiments show, then, that antibodies injected into the mother are transmitted to the offspring. This being the case, it is but reasonable to expect that some of the protective substances ordinarily present in the normal mother's blood should likewise reach the child through the milk. Experiments have shown this also to occur. Moro found that the bactericidal power of the blood-serum in breast-fed children was distinctly greater than in those artificially fed. Further confirmation was afforded by the fact that this difference rapidly disappeared when the bottle-fed infants were put back to the breast."

The prevention of disease in the infant is raised to its highest standard by maternal lactation. The organisms of its gastrointestinal canal are kept under control; the barriers to infection that the respiratory tract and pulmonary alveoli offer are well armed with antitoxic bodies; the blood itself is destructive to pathogenic organisms, and the infant is thus protected against those diseases which, even if recovered from, we have

seen, leave enfeebling lesions, fatty and fibrous degeneration, in those organs upon which his health in after years and the duration of his life depend.

In the child beyond the nursing period the problem is more difficult. The fatal "second summer" recalls the sins of the milkman, the filth of the cowshed, and of the vessels in which the milk is transported and kept amply long enough to favor the growth of the oft-present Shiga bacillus, the virulent *Bacillus coli,* and even at times the streptococcus. The correction of these and many other factors replete with danger to the child, and which surround it on all sides, offers the only resources to diminish not only the mortality of children's diseases, but their occurrence, besides safeguarding health and longevity in after years. The good already done by our profession in this direction is incalculable. Briefly, public, home, and school hygiene, in the light of the facts I have submitted, not only serves to protect life for the moment when the child is concerned, but its entire career as a healthful individual, while enhancing greatly his chances for a long life.

It now becomes a question whether our resources are such as to enable us to raise, where functional hypoadrenia exists, the autoprotective resources of the child, sufficiently, perhaps, to enable it to resist infection successfully. The influence of many toxins and drugs on the adrenals points clearly to overactivity under their influence. In 1903 ("Internal Secretions," vol. i) I referred to mercury as occupying "a high position among the stimulants of the adrenal system." Now, C. R. Illingworth ("The Abortive Treatment of Specific Febrile Disorders," etc., London, 1888) and others have found the **biniodide of mercury** extremely efficient in aborting scarlatina, diphtheria, measles, variola, varicella, pertussis, parotitis, and many other infections. The great vogue of **calomel** among the physicians of the past generation may have found its *raison d'être* precisely in just such an action—which I have myself observed. **Arsenic** is a familiar agent in the abortive treatment of malaria in Africa, and, as Surgeon-General Boudin states, in many other diseases. The remarkable results of Petresco with large doses of infusion of **digitalis** in pneumonia have only been tentatively explained. But if we realize that division of the path to the adrenals arrests and prevents the effects of digitalis, as is now well known, there is good ground for the belief that the prevailing conception of the action of this drug is erroneous, and that it is by stimulating the adrenals that it acts, at least in part. In view of the immunizing action of the adrenals, therefore, we can realize how **digitalis** could be of use in this infectious disease, and how it might prove useful in aborting any pulmonary disorder due to pathogenic organisms.

Very remarkable in this connection is the action of **thyroid gland** 1 grain (0.06 Gm.), **adrenal gland** 2 grains (0.12 Gm.), and **Blaud's pill** 1 grain (0.06 Gm.) in a capsule three times daily, previously referred to. Given during meals to a debilitated child of 10 or 12 years, it seems promptly to start the vital machinery on a new lease of life—where, of course, the demands of hygiene are adequately met. **Meat** is of value here, while **milk,** the fluid portion of which gives the test for oxidases, and which, as I have shown elsewhere, depends upon the adrenal secretion for its ferment (adrenoxidase) is also of great value. **Digitalin** or **strychnine** in small doses is added if the heart

is weak or to increase the oxygen intake. All these agents tend, by keeping up a slight hyperemia of the adrenals (and of the other organs acting in conjunction with it), to augment the efficiency of the child's defensive resources.

In the **adult** functional hypoadrenia may have persisted from childhood. Here the measures just suggested for children apply as well not only as preventives where infection threatens, or as abortive treatment, but also to raise the efficiency of the adrenals and the general health of the individual to the normal plane. It is probable that most tonics exert their beneficial influence through the adrenals. That "tonic" doses of **mercury**, *i.e.*, minute doses, are efficient is well known; we have seen that it is a powerful adrenal stimulant. In toxic doses, in fact, as observed by Moliné (Bull. gén. de thérap., Apr. 8, 1906), it causes intense congestion and even hemorrhage of the adrenals.

While there is no doubt that **meat** in excess is harmful, it is undoubtedly true that, as Lorand (*loc. cit.*, p. 313) states, undernutrition through lack of the necessary proteids in the diet increases the liability to infection, as I several years ago pointed out. Lorand refers to personal cases of tuberculosis arising from a purely vegetarian diet. On the other hand, Richet and Héricourt (Lancet, Jan. 7, 1911) obtained remarkable effects from a diet of raw meat in enabling animals to resist tubercle infection by inoculation, and raw meat has become an important factor in the treatment of this disease. Grawitz (Klinische Pathologie des Blutes, 3d ed., 1906) also found that a purely vegetarian diet predisposed to anemia. We have seen that the adrenals supply the blood its albuminous hemoglobin, a deficiency of which is an important feature of anemia. Did we live where pathogenic bacteria do not flourish, we might safely undertake to adopt vegetarian principles; but a reasonable amount of meat, by keeping our autoprotective organs, and particularly the adrenals, active, serves a very useful purpose.

The influence of excessive fatigue on the adrenals, we have seen, is such as to weaken greatly their functional activity and, therefore, the oxygenizing and immunizing functions of the blood. The main harmful feature in this connection is the *relative* deficiency of rest, which means, from my viewpoint, the inadequate opportunity afforded the adrenals to recuperate. This, of course, should be proportionate to the amount of strain imposed upon these organs, and the resistance of which they are capable. It is probably owing to lack of this that apparently strong men are often the first to "give out" in forced marches. The physical examination being based mainly upon the *status presens*, and the adrenals being necessarily (for we are now dealing with a new line of thought) overlooked as factors, there is marked inequality in the resistance of the men to strain. This applies as well to the pathogenesis of chronic disorders. In a personal analysis of 40 cases of hay fever, for instance, the severity of the disease corresponded to a considerable degree with the number of children's diseases the patient had had, the worst cases having had six of these diseases in comparatively quick succession.

This suggests the need of ascertaining the number and severity of children's and other diseases to which the recruit has been subjected and to add this factor to others in deciding upon his admission to the service or the arm to which he is to be assigned. The

mounted man suffers less from actual fatigue than the infantryman, who must carry his accoutrements, arms, cartridges, etc., aggregating in some armies as much as 70 pounds. When, besides, defective or poor food, impure water, exposure, etc., and other frequent accompaniments of a campaign are taken into account, one need not wonder that disease is a far greater factor as causes of debility and death than wounds.

Briefly, fatigue should be considered, owing to its inhibiting influence on the adrenals and the immunizing process in which they take part, as an important predisposing cause of disease. The periods of rest should be so adjusted, therefore, as to counteract this by far the most destructive factor of active warfare. In civil life, such hardships are seldom endured, but here, likewise, much could be done to prevent infection by means calculated to insure the functional integrity of the adrenals.

To stimulate the adrenal functions when marked fatigue prevails would, of course, only aggravate the hypoadrenia after, perhaps, a period of temporary betterment. The powdered **adrenal substance** should, on the other hand, judging from the effects of injections of adrenal extracts in experimentally fatigued animals, serve a useful purpose.

In **old age** the ductless glands assume such importance that a valuable work has been written by Lorand ("Old Age Deferred," F. A. Davis Co., Phila., 1910) to indicate how the functional activity of these organs could be preserved in order to retard the ravages of age beyond the fifth decade, while prolonging life. The reader is therefore referred to Dr. Lorand's volume for a mass of information which cannot be considered here.

The adrenals, as shown by the plate opposite page 460, are deficient in circulatory activity, and, therefore, unable to sustain functional activity of all organs up to its former standard. It becomes a question whether, realizing this fact, we should by artificial means excite the adrenals to greater activity. That such a step might shorten life instead of prolonging it, is probable. In the first place, the frequent presence of arteriosclerosis in the aged counsels prudence; in the second place, to activate the adrenals would only hasten their degeneration by imposing a greater wear and tear upon them. Drugs capable of enhancing adrenal activity had, therefore, better be avoided in the aged.

Far better is it to *compensate* for the loss of efficiency of the adrenals by supplying to the blood, through a suitable **diet,** substances which contain the adrenal principle. If my opinion that spermin owes its virtues to the adrenal principle it contains is warranted, we can understand why Brown-Séquard rejuvenated himself by means of testicular juice injections (I saw him at the time and can testify to its wonderful effects upon him), since he enriched his blood with the *pabulum* of oxidation, metabolism and general nutrition, without impairing his adrenals. With advanced knowledge we need not follow his example. We have seen that **milk** contains the adrenal principle, and that all animal tissues owe their functional activity to its presence. In milk, **buttermilk** especially (since it is almost pure plasma), we have a ready and inexpensive means to compensate for deficient adrenal activity. If debility and other signs of functional hypoadrenia prevail, I advocate the daily addition to the plain, though varied, diet to which elderly people should restrict themselves of the **expressed juice** (uncooked) of one pound

of fresh beef daily, taken in soup, if distasteful otherwise, and salted to taste. This is a powerful agent for good which is well borne by the stomach, and which more than compensates for the weakened adrenals, since it rapidly restores strength and vigor—provided, of course, harmful influences in other directions are avoided, and a hygienic mode of life, with reasonable out-of-door exercise, prevails.

In matters sexual, aged men should be extremely reserved, since the waste of seminal fluid to them means waste of life substance, replaced with difficulty and never in abundance.

> Case of total absence of the adrenals in a woman, aged 52, who, in September, 1902, noticed that her hands frequently became cold and discolored. In January, 1903, the joints of fingers and wrists became stiff and swollen; during April she suffered from pleurisy, and one month later noticed that the skin of the entire body was becoming darker (Addison's disease), the abdomen enlarged, and she discovered a slight discharge from the umbilicus. The skin grew darker and darker (scleroderma). The joints of the fingers and wrists became almost immovable and several of the finger-joints ulcerated, attended with a purulent discharge (Raynaud's disease). She suffered intensely with the pain, cold and stiffness in all the joints of the extremities. She became emaciated and the whole integument became dry, hard, and cold.
>
> Under treatment with desiccated adrenal immediate improvement was noticed. The ulcerated joints healed, pain in them ceased, and they became more limber. The skin softened and grew lighter. Improvement continued for about one year when the patient complained that the powder disturbed her stomach and refused to continue the drug. From this time she grew gradually worse and the previous ulcerated, stiff, cold, and painful condition of the joints returned, associated with the increased pigmentation and hardness of the skin. She died suddenly, December 14, 1906. At the autopsy no trace of the adrenals could be found. C. R. Love (N. Y. Med. Jour., Jan. 29, 1910; Jour. Amer. Med. Assoc., Feb. 12, 1910).

PROGRESSIVE HYPOADRENIA.—In this condition, local lesions, tubercular, syphilitic, sclerous, etc., progressively inhibit the functions of the adrenals until they fail, destroying life. *Addison's disease,* treated separately on page 356 of this volume, by Professor J. P. Langlois, of Paris, to whose labors I have repeatedly referred in the foregoing pages, is the most important syndrome of this group. In addition is the group of *malignant tumors* which, though presenting the chief phenomena of the former and, therefore, those of hypoadrenia, include various symptoms peculiar to malignant neoplasms which warrant the recognition of an autonomous syndrome complex.

CANCER OF THE ADRENALS.—Primary malignant tumors of the adrenals are generally regarded as very rare, but it is probable that when the symptomatology of these growths will be known by the profession at large, a certain proportion of deaths now attributed to Addison's disease in adults and to asthenic disorders in children will be found to be due to this class of growths. Addison, in fact, included these neoplasms among the etiological factors of the disease which bears his name, but it is now plain that the two syndromes differ in many respects, and that the treatments indicated—medical in the one and surgical in the other—imposes the need of recognizing malignant neoplasms of the adrenals as distinct morbid entities.

VARIETIES.—Primary malignant tumors of the adrenals are of the various forms of sarcoma, those most fre-

quently met with and which occur, in the majority of instances, in infancy, childhood and adolescence; *carcinoma*, which occurs, as a rule, in adults or aged subjects. Among the rarer varieties may be mentioned the malignant *hypernephroma* and a class of tumors termed by Prudden *hemorrhagic adenoma*.

The sexes are affected about equally, but they appear much earlier in females than in males. Carcinoma may develop from hypernephroma.

[Sixty-seven collected by Ramsay from literature, including 30 of sarcoma and 37 of carcinoma. This would tend to suggest that the two forms occur about evenly. C. E. DE M. S.]

Primary tumors of the adrenals are very infrequent. In the statistics of the Pathological Institute of Geneva, out of 7249 autopsies performed from Oct. 1, 1876, to Oct. 1, 1903, the proportion was 0.6 of 1 per cent. Dupraz (Revue méd. de la Suisse Romande, Mar. 20, 1906).

Study of the collection of kidney tumors in the Jewish Hospital at Berlin, 103 in all. No less than 69 belong to the group of hypernephromas. In two the writer found unmistakable evidence that true carcinoma had developed out of a hypernephroma. Displaced suprarenal germinal matter had lodged in the kidney in early embryonic existence, a hypernephroma had developed from this, and the carcinoma from the parenchyma of the hypernephroma. The writer does not maintain that embryonal displacement of germinal matter is the only cause of these cancers, but in these cases it was evidently the first embryologic cause, without which these carcinomas would never have developed. The same applies also to some cases of sarcoma developing in a hypernephroma which are in the collection. The sarcoma had developed from the stroma. Neuhäuser (Archiv f. klin. Med., Bd. lxxix, Nu. 2, 1906).

SYMPTOMS.—As a rule, the general phenomena develop insidiously, the adrenal lesion being well advanced when they begin to appear. The strength wanes more or less rapidly; the weight graually decreases; the pulse and cardiac action become increasingly weaker and more rapid; the temperature shows exacerbation of a couple of degrees at times, but in the advanced cases is usually subnormal; the appetite decreases; digestive disturbances, such as nausea, vomiting, flatulence and diarrhea, are commonly observed. Anemia is sometimes manifest, the hemoglobin being often reduced to 50 per cent., and the red corpuscles to 3,000,000 or less. Cough, with bronchial râles, localized dullness and hemoptysis are occasional complications, while dyspnea and increase of the number of respirations are apt to occur in advanced cases. The skin may remain normal, but various degrees of pigmentation, ranging from slight icterus to actual bronzing, are observed in the majority of cases. The typical facies may alone be present in cases of primary carcinoma.

[This symptomatology is based on a personal analysis of 60 reported cases of primary malignant tumors of the adrenals. The phenomena are clearly explained by the functions I attribute to the adrenals. Being the purveyors of the secretion which—as the albuminous constituent of hemoglobin—sustains oxygenation and metabolism and, therefore, nutrition, increasing emaciation, weakness, hypothermia, the decrease of hemoglobin, etc., are but normal results, all the other phenomena being secondary thereto. The cases in which no pigmentation of the skin occurs are usually those in which but one adrenal is involved. C. E. DE M. S.]

Case of primary sarcoma of the adrenal glands which did not show symptoms of Addison's disease. The existence of the tumor was not suspected until after the death of the

patient. The symptoms present suggested carcinoma of the stomach, though the more characteristic symptoms were absent. Both adrenal glands were sarcomatous. Blackburn (Amer. Jour. Med. Sci., Aug., 1906).

Case of myxosarcoma of the suprarenals, in which the patient had been suffering from gastrointestinal disturbances, a sense of weight in the abdomen after meals, and later from a pain at the base of the chest on the same side. This pain resembled that of muscular rheumatism, and was especially severe at night. These symptoms gradually increased, followed by intestinal hemorrhage, and edemas at the ankles. The urine had always been normal, and there had been no vomiting. The tumor could be distinctly felt on the right side, was firm in consistence, and reached from the iliac crest to the costal arch; the right lobe of the liver was found pushed upward. The diagnosis of a renal tumor was made and the operation revealed a large bilobed growth, partly softened in the center, which occupied the suprarenal gland and did not involve the kidney. On further examination the tumor proved to be a myxosarcoma. Sicuriani (Riforma Medica, Nov. 4, 1905).

All these phenomena are seldom witnessed in a single case. As a rule, after a period of progressive emaciation and adynamia, a tumor can be detected by palpation posteriorly below the costal margin, close to the vertebral column. The mass at first follows the respiratory movements and recedes under pressure, but it eventually becomes fixed and immovable.

In some cases, especially in infants, the tumor cannot be detected in this manner, but the abdomen gradually enlarges with a steady increase of the line of dullness, though, perhaps, no other symptom be discernible. When the outline of the growth can be clearly followed with the fingers, its border is nodular, as in hepatic cancer, but smooth.

Pain is sometimes complained of; it may be located in the region of the tumor; or, radiating upward or across the back, it may extend to the shoulders.

[The pain has been attributed to the phrenic nerve, but a clearer explanation is the effect of the traction by the tumor, upon the sympathetic ganglia and through the greater splanchnic, upon the sympathetic chain, which is merged in with the mass of nerves, including the brachial plexus, in the tissues of the shoulders. C. E. DE M. S.]

Pressure symptoms are apt to complicate a case of long duration. Ascites, general edema, or edema of the ankles or legs are commonly observed in such cases, due notably, in most instances, to pressure upon the inferior vena cava. Gangrene of the feet has also been observed. In carcinoma metastasis is most common in the liver and lungs; in sarcoma it is not quite as frequent and occurs in most cases in the liver and kidney.

Death may occur suddenly, preceded by very few of the above symptoms, especially the sarcomata of infants. In the majority, however, especially in adults, the morbid symptoms gradually develop and the asthenia increases until unconsciousness, labored breathing and coma terminate in death.

Infants may also suffer from a congenital type of adrenal tumor which simultaneously invades the liver. It is encountered as a congenital tumor during the first week of life. The abdomen becomes increasingly distended; there is moderate emaciation, but no jaundice, pigmentation, ascites, or even pain, the child nursing almost up to the time of death.

Series of six cases, including a personal case, showing that congenital

sarcoma of the adrenals and liver constitutes a special type of malignant disease with its own peculiar symptoms and pathological findings: Swelling of the abdomen occurred within a period ranging from birth to five weeks, thus indicating the congenital nature. The infants lived from one to sixteen weeks, thus showing great malignancy. The increase of growth could be discerned from day to day, thus illustrating rapid development. All were females. The entire normal liver structure was practically destroyed in all. The suprarenal growth exhibited the peculiarity of being very hemorrhagic. No other part of the body was involved by the new growth. William Pepper (Amer. Jour. Med. Sci., Mar., 1901).

Case of a female child, aged 7 weeks, who presented a swelling of the belly. On examination of the abdomen the superficial veins were found distended, and the epigastric and both hypochondriac regions were greatly enlarged and prominent. The surface of this enlargement was perfectly smooth and uniform, presented no irregularity, and no pulsation was visible. Careful palpation revealed the presence of a solid mass which was movable during respiration, and which was evidently an enlarged liver. A second enlargement occupied the left half of the abdomen. It was also movable during respiration. The two swellings appeared to be quite distinct from each other. The blood was frequently examined, and at first showed decided leucocytosis, which, however, disappeared. The patient steadily lost strength and emaciation began, and then slight edema of the lower limbs appeared. The abdomen became increased in girth, and gradually the two areas of enlargement and dullness descended into the right and left iliac fossa respectively. A provisional diagnosis of splenic anemia with coincident hepatic enlargement was made. The post-mortem examination revealed the fact that the enlargement of the liver was due to the presence of numerous sarcomatous nodules. The primary growth was discovered in the right adrenal. John Orr (Edinburgh Med. Jour., Sept., 1900).

Case of primary malignant tumor of the adrenal occurring in a child 2 months old. The parents first noticed a slight swelling of the abdomen, which increased rapidly. On examination the writer found distinct enlargement, some edema of the abdominal walls, and the superficial veins much distended. On palpation a hard, smooth mass was felt, chiefly in the right side of the abdomen, extending from the costal margin down to the right inguinal region, passing deeply into the right flank and filling up the whole space between the ribs and the iliac crest. In the right inguinal region a firm edge was felt, which could be traced from Poupart's ligament toward the navel, passing below the navel and then gradually ascending. To the left of the navel a notch could indistinctly be felt, but it was not possible to distinguish two separate masses. The length of the tumor mass in the median line was 16 cm., the distance from the interclavicular notch to the umbilicus was 21.5 cm., and the greatest circumference of the abdomen was 46 cm. The uniform tumor apparently represented the liver. The red blood-corpuscles numbered 2,800,000; the white 11,000, of which 79 per cent. were polymorphonuclears, 18.5 per cent. small mononuclears, 2.3 per cent. large mononuclears and transitionals, and 0.2 per cent. eosinophiles. The child died in convulsions six days after it was seen the first time. The autopsy disclosed a tumor of the left adrenal gland and a very much enlarged liver. The liver was cirrhotic and fatty, and contained numerous masses of cells, the same as those in the adrenal tumor. Amberg (Archives of Pediatrics, Aug., 1904).

DIAGNOSIS.—The diagnosis of malignant tumor is not difficult when the tumor is sufficiently large to be discovered by palpation, especially when

paresthesia over the kidney is present. This and the asthenic phenomena point clearly to the adrenals, especially if jaundice or any pigmentation of the skin be present. Unfortunately, the morbid process is far advanced, as a rule, when these signs appear. The tumor has been mistaken for *psoitis* and *abscess*. From *hepatic cancer* it differs in that the surface of the tumor is smooth instead of lobulated. Of course, the possibility of metastasis in the liver, its most frequent seat, must be borne in mind. *Hydatid cyst* may be suggested, but the absence of the hydatid thrill and other typical symptoms will avoid error. A projecting and *enlarged gall-bladder* is sometimes simulated by an adrenal tumor capable of displacing the intestines anteriorly; but the latter are much less tense than such a gall-bladder. *Abdominal aneurism* may be suggested,but the absence of aneurismal bruit and the absence of all other signs of adrenal growth eliminate this source of error. In *renal cancer* or *renal hypernephroma* hematuria and other evidences of renal disorder are usually present, while they are more likely to be absent in malignant growths of the adrenals. Pain occurs earlier than in renal tumors, while febrile disturbance is rare in the latter.

> Two symptoms point to involvement of the suprarenal gland: (*a*) paroxysms of pain and paresthesias in the absence of a palpable tumor, and (*b*) a febrile course. The painful paroxysms in renal as well as suprarenal tumors are due to the extension of the neoplasm to the roots of the lumbar plexus. In suprarenal tumor this may occur quite early, owing to the immediate vicinity of these structures. On the other hand, in renal tumors the invasion of the capsule usually takes place at a late period, when the growth has reached so considerable a size as to become palpable. The fact that fever occurs in cases of suprarenal tumors has hitherto been unknown. The writer observed it in 57 per cent. of his cases, while in renal tumors it was present only in 1 to 2 per cent.
>
> Another apparently characteristic fact in differentiating from renal tumor is that the adrenal growth tends to approach more nearly the median line—in the region from the seventh to the ninth costal cartilages; while the primary tumor of the kidney appears first in the region from the ninth to the eleventh. Tumor of the adrenal at the time of its presentation beneath the margin of the ribs appears broader than does that of tumor of the kidney, and the lower contour of the tumor of the adrenal is much less rounded than is that of the kidney. J. Israel (Deut. med. Woch., Nu. 44, 1905).

[The emphasis laid by Israel on the presence of fever in adrenal malignant neoplasms affords striking proof of the correctness of my contention that the adrenals, through the rôle of its secretion in oxidation and metabolism, was the active organ in fever—a process which pathologists have totally failed to explain. C. E. DE M. S.]

Leucocythemia is sometimes simulated, but the absence of myelocytes and other characteristics soon eliminate this disease.

Ecchymosis of the orbit of unaccountable origin in infants and young children, or tumor of the orbit should cause careful search for other manifestations of malignant hypernephroma of the adrenals.

TREATMENT.—Removal is the only resource, but, as a rule, the result is unsatisfactory, owing to the fact that the presence of the growth is recognized only through metastasis; or when it has developed to a marked extent, and produced either through metastasis, pressure, etc., disorders in other parts of the organism which cannot be reached.

Three cases of adrenal tumor treated by **removal.** One was in a woman, aged 47, on whom the writer operated in 1891, who died of recurrence of sarcoma and exhaustion several months after the operation. The suprarenal growth was so firmly fixed to the top of the kidney that that organ had to be removed as well. The second case was that of a woman, aged 62, on whom he operated in 1897, and who is still living and well, the tumor removed having been a struma lipomatosa suprarenalis, as described by Virchow. In this case only a wedge-shaped piece from the top of the kidney was removed with the tumor, a procedure followed by no morbid symptom. The third operation, by his colleague, Mr. Ward, was for a sarcoma of the adrenal in a child, aged 12 months. The child died from shock within a few hours.

Of 9 cases, including his own, 5 recovered from the operation and 4 died. The true secret of success lies in operating at an early stage of the growth, as in the writer's second case. Mayo Robson (Med. Press and Circular, Aug. 23, 1899).

Removal of an adrenal myxosarcoma from a man of 50. The tumor weighed about seven pounds when removed. There was no cachexia, mononuclear leucocytosis or other symptoms pointing to the suprarenals. The sound suprarenal must have acted vicariously for the affected organ. The patient had recovered when last seen, two months after a two-hour operation. F. Sicuriani (Riforma Medica, vol. xxi, No. 44, 1905).

Cases in which the tumor involves one adrenal only, as suggested by the absence of symptoms of adrenal insufficiency, marked asthenia, emaciation, hypothermia, etc., and the presence of a tumor and hyperesthesia on one side only, offer a better chance of success, since they indicate that the other adrenal will probably be able to subserve alone the needs of the organism. The chief difficulties encountered in the course of the operation are a marked tendency to hemorrhage, owing to the friability of the morbid tissues.

HYPERNEPHROMA.—This name has been given to tumors formerly considered as lipomata, adenomata or myxomata, but shown by Grawitz in 1883 to be developed from adrenal tissue, either within the adrenals themselves or in the kidneys, the walls of blood-vessels or other structures in which "adrenal rests" (fragments of misplaced adrenal tissue) or "aberrant adrenals" occur.

From my viewpoint, these so-called "adrenal rests"—found in 90 per cent. of all autopsies by Bayard Holmes, at least once a week by Grawitz in his autopsies, etc.—are not misplaced fragments of adrenal tissue; they belong normally to the kidney.

[I have shown (Monthly Cyclo., June and July, 1909) that what has been termed the internal secretion of the kidney is a product the properties of which correspond with those of the adrenals, and (see "Internal Secretions," 3d ed., p. 289, 1908) that the kidney and the adrenals were governed by the same nervous structures, being thus closely linked functionally. Under the influence of centric impulses the so-called adrenal rests and the adrenals are both caused to increase their secretory activity and to enhance the intrinsic metabolism of the tissues they supply. On the whole the "adrenal rests" are but local aggregates of the chromaffin substance found in all sympathetic structures. C. E. DE M. S.]

Study based upon 48 hypernephromata. Thirty-four of the tumors were removed at operations in the Mayo Clinic, and 14 were unreported cases gathered from outside sources. The following general conclusions are drawn from this study: 1. Most, if not all, so-called "adrenal rests" are probably of Wolffian origin. 2. There is almost no evidence, embryological or histological, in support of Grawitz's hypothesis

that the so-called hypernephromata have their origin in adrenal rests. 3. There is much evidence that the so-called hypernephromata do arise (according to Stoerk's hypothesis) from proliferations of the adult secreting epithelium of the convoluted tubules. 4. There is much evidence that the so-called hypernephromata do arise from islands of nephrogenic tissue (primitive renal blastema). Such tissue is sometimes present in the adult kidney and appears capable of forming tumors of non-infiltrating mixed cordon, tubular, papilliform, and sarcoma type characteristic of the so-called hypernephromata. L. B. Wilson (Jour. of Med. Research, Jan., 1911).

Hypernephromas are relatively common in the kidney, constituting, as shown by Albarran and Joubert, 17 per cent. of all renal tumors; they are much less frequently found in the adrenals proper, or in other organs, such as the uterus, ovary, the broad ligament. Microscopically they present the typical characters of the adrenal cortex, and closely, as a rule, infest vascular channels. These vessels and adjacent tissues usually contain a colloid material similar to that found in the thyroid, or secreted by the adrenals. They are benign at first and become troublesome—sometimes after many years—mainly on account of their size, which sometimes reaches that of a child's head, but the pressure they exert on surrounding structures, their tendency, even when benign, to metastasize in the lungs, bones, brain, give them their malignancy.

Case of hypernephroma encroaching upon the heart. The earlier symptoms were cardiac with great weakness, one and one-half years before urinary phenomena occurred. Then followed hematuria, and a tumor was discovered in the left kidney; it proved on removal to be a hypernephroma from an aberrant suprarenal tissue proliferating into the ascending vena cava with a tumor thrombus up in the right auricle. Skipping the right ventricle, it had proliferated into the pulmonary artery. Kirschner (Berl. klin. Woch., Sept. 25, 1911).

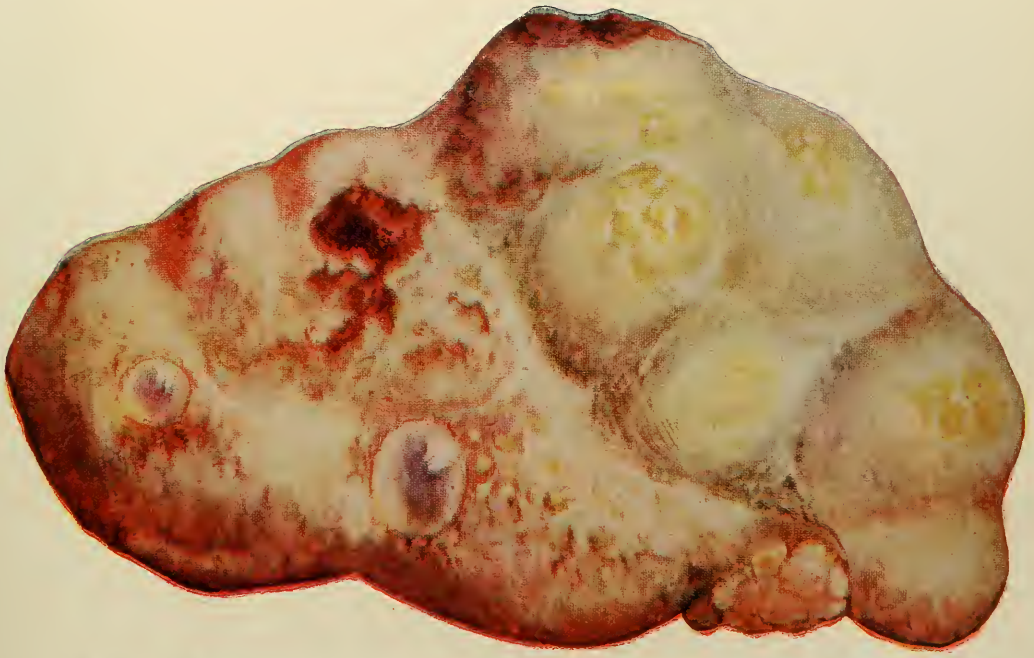
SYMPTOMATOLOGY.—Before the local symptoms of the tumor appear—when any are clearly discernible—it evokes phenomena which are diametrically opposed to those of Addison's disease, and which correspond with increased nutrition and a stimulation of growth such as that produced by thyroid preparations in cretinism.

[This action on growth and its resemblance to that brought about by thyroid overactivity has imposed itself upon investigators quite independently of my own view—advanced in 1903 ("Internal Secretions," vol. i, pp. 146-152), that it was in great part through the adrenals, *i.e.*, through incidental stimulation of the adrenal center by the thyroid secretion, that the benefit of thyroid in cretinism was produced. The confirmatory evidence it affords is self-evident. The excess of adrenal tissue which constitutes hypernephroma brings about the general phenomena of overnutrition merely because it awakens excessive metabolism precisely as if the thyroid overactivity had done so by exciting the adrenal center. C. E. DE M. S.]

The symptomatology varies considerably in different cases and suggests that several types exist which our present knowledge does not enable us to discriminate. Some of these exhibit such malignancy that they have been grouped in a separate class. Beginning with hypernephromas of the adrenals proper, we will first review this class of cases.

MALIGNANT HYPERNEPHROMA OF THE ADRENALS.—This growth occurs, as a rule, between the first and eighth year, especially in girls of the latter age, and causes premature development so marked, in some instances, that the child appears, as to

Appearances of kidney and tumor on section through the long axis of the organ and its pelvis. (Annals of Surgery, Dec., 1906.)



Hypernephroma. Showing the external appearance of the kidney and tumor about one-third smaller than at the time of operation. (Annals of Surgery, Dec., 1906.)

size and development, twice or three times its true age. The face, genitalia, and pubis are covered with abundant growth of hair, the external genitalia being as fully developed as in the adult. The body is obese, the appetite and thirst excessive, although gastric disorders, including stubborn vomiting, are common. The skin may be swarthy or dark-hued, as in a brunette, but not bronzed as in Addison's disease. Such children are usually cross and sullen, unlike obese children, in whom the obesity is due to deficient fat catabolism. These primary growths of the adrenals, which are usually observed in girls, are of slow development, and years usually elapse before metastasis and pressure phenomena—those which give the growth its malignancy—appear.

The abnormal growth of the child may suggest gigantism or acromegaly, due to some disorder of the pituitary body, but the characteristic growth of the extremities, the absence of obesity in these disorders do not occur in hypernephroma. An elevated temperature is often observed in these cases.

Removal of 14 cases of malignant hypernephroma. Fever was a prominent symptom, unaccounted for by any complication. This reaction may be early, intercurrent, or late. It sometimes is the first clinical evidence of the malady, or it may accompany the evolution of the disease; or it may be a terminal symptom. The type may be hectic, recurrent, or one associated with hematuria; or the fever may be atypical. The reaction cannot be connected with liberation of bacterial toxins or absorption from necrobiotic tissues. It doubtless accompanied the evolution of all malignant growths, but the *rationale* is not clear. Israel (Deut. med. Woch., Jan. 12, 1911).

[The occurrence of fever in these cases is clearly accounted for by my views. As shown in "Internal Secretions" (vol. ii, p. 1907), the pituitary body contains the sympathetic center besides the adrenal center. During the first or erethic stage, therefore, the adrenals, the secretion of which sustains oxidation and metabolism, and which alone cause overgrowth in malignant hypernephroma, are not alone overactive, but the arterioles, which the sympathetic governs, also. The blood is not only abnormally rich in oxygenizing properties, therefore, in this disease as it is in malignant hypernephroma, but it is also driven with excessive energy into the tissues, particularly in the long capillary loops of the extremities. Hence the difference between the phenomena of overgrowth in the two diseases and the elevated temperature. C. E. DE M. S.]

Tumor of the orbit in infants and young children should arouse the suspicion of metastases from an adrenal growth. If an abdominal tumor be found, it is almost certainly of adrenal origin, and this would be still further corroborated by enlargement of the preauricular glands, which renders the diagnosis of sarcoma of the orbit unlikely. Chloroma presents almost identical growths, being associated with tumors of the orbit in two-thirds of the cases, with exophthalmos usually as the first symptom, but this may be excluded in the absence of leukemic changes in the blood. Myeloma may cause bony growths about the skull, but is exceedingly rare in childhood; the presence of the Bence-Jones body in the urine would render the diagnosis of myeloma certain, while its absence is not conclusive. The authors state that abdominal tumor associated with precocious maturity is practically certain to be of adrenal origin, if tumors of the ovaries or a retained testis can be excluded. Other adrenal tumors cannot be distinguished from tumors of the adjacent tissues, especially of the kidneys. Tileston and Walbach (Amer. Jour. Med. Sci., June, 1908).

Case of tumor of the adrenal gland with metastasis in and about the orbit. The following are the char-

acteristic symptoms usually found in infants or young children: Ecchymosis of the eyelids, accompanied by exophthalmos, suddenly appears; it may be followed by growths about the orbit. It is usually confined to one side. The glands throughout the body are apt to be enlarged. Examination of the abdomen may reveal a tumor in the region of the kidney, or a mass may be felt in other parts of the abdomen. The blood shows secondary anemia. The urine is usually free from blood and albumin. Most of the reported cases have been under 4 years of age. The course of the disease is rapid, death resulting from cachexia and anemia.

The author also calls attention to the following: 1. Tumors of the orbit in young children, especially if accompanied with ecchymosis of the lid, should arouse suspicion of metastasis from an adrenal growth. 2. The microscopic examination of specimens shows a characteristic rosette formation of cells. 3. This form of tumor arises from embryonic nerve-cells of the adrenal gland. Quackenbos (Arch. Ophthal., Sept., 1910).

Case of malignant hypernephroma in a boy of 9 years, who had always been pale and weak. Six weeks after an acute pericarditis the symptoms of the malignant disease became apparent and the tumor soon penetrated into the thorax. Three other cases are on record in which a malignant hypernephroma developed in a child. The other children were between 2 and 5 years old; in one the tumor had developed on a horseshoe kidney. All were distinguished by extreme malignancy, but no hematuria was observed. In the 222 cases of hypernephroma the writer has found on record a traumatic factor was evident in only eight instances. Franck (Beiträge z. klin. Chir., Jan., 1910).

Infants and young children are also subject to a form of primary malignant tumor of the adrenals, described by Hutchinson, in which, even before the neoplasm, which grows with great rapidity, can be felt in the renal region, there appears a spontaneous—sometimes traumatic—ecchymosis of one or both eyelids, soon followed by (usually unilateral) exophthalmos and metastasis in the skull, and often in other bones, especially the ribs. The preauricular lymph-nodes, and those behind the angle of the jaw, are enlarged, and the whole temporal region eventually becomes the seat of a malignant growth. Pain in this location and optic neuritis with amblyopia may complicate the case. Death occurs early from anemia and cachexia.

Out of 196 cases of kidney tumor 146 were hypernephromata—that is, almost exactly 75 per cent. The remaining 25 per cent. are made up mostly of sarcomata, to a much less extent of squamous epitheliomata of the pelvis, while a true carcinoma of the kidney, apart from hypernephroma, is a very great rarity, or, possibly, does not exist. The kidney tumors of children are practically all sarcomata; there is but one case on record of a true hypernephroma in an infant, and, as was long ago pointed out by Küster, malignant disease of the kidney is a disease of earliest childhood and middle age, affecting but little young adults and the aged. Hence, we may lay it down definitely that hypernephroma is the common kidney tumor of adults, and, conversely, that any given kidney tumor in an adult is much more likely to be one of this type than anything else. This is the only etiological fact bearing on the disease which we can regard as absolutely definite. Trotter (Lancet, June 5, 1909).

Adrenal carcinoma shows two entirely distinct syndromes and pathological states, according to which adrenal is the seat of the primary tumor. On the left side secondary deposits occur in the liver, ribs, cranial bones, and in the thoracic duct and some of its tributaries. On the right side the primary growth generally attains a larger

size, and oftener remains localized to the abdomen. It tends to involve the kidneys by direct extension into their pelves, stretching out the kidney substance over it, but, as a rule, being easily separated. Secondary deposits occur on the upper surface of the liver, in both lungs, occasionally in the cranial bones, and also in the right lymphatic duct and some of its branches. The lymphatics of the right suprarenal are tributaries of the right lymphatic duct, and do not, as is usually stated, follow a course similar to that of the lymphatics of the left adrenal, viz., join the lumbar glands. Deposits in the cranial bones often cause exophthalmos, this usually occurring first on the same side as the primary growth. Ecchymoses into the eyelids may occur and lead to confusion of the disease with chloroma and infantile scurvy. The tumor in these cases involves the medulla of the adrenal, and there are reasons for believing that it is of carcinomatous nature. No pigmentation or evidence of a premature sexual development, such as have been described as occurring in cases of carcinoma of the cortex of the suprarenal, were found in any of the cases studied. R. S. Frew. (Quarterly Jour. of Med., Jan., 1911).

HYPERNEPHROMA OF THE KIDNEY.—It is to renal growths developed from the so-called "adrenal rests" that Grawitz, in 1883, gave the name "hypernephroma." They occur not only more frequently in the kidneys than elsewhere in the body, but constitute a large proportion of all renal tumors, *i.e.*, 17 per cent.

SYMPTOMATOLOGY.—Hematuria is often the first and the most frequently observed symptom of renal hypernephroma, having been noted in 90 per cent. of all cases. The hemorrhages are usually severe and occur intermittently, weeks and even months elapsing between them. Worm-like clots—thus shaped during their passage through the ureters—are often passed. During the intervals the urine is either clear or it may contain red corpuscles. The hematuria is increased by exercise and by manipulation of the region overlying the growths if the latter is sufficiently large to be felt. It may be the only symptom of the growth or precede the detection of the latter by palpation as much as ten years. As a rule, however, the tumor (which occurs in 80 per cent. of all cases) is sufficiently large to be detected much earlier, and sometimes immediately after an attack of hematuria. It is located in the loin, often on the right side, and two or three finger-breadths below the costal margin. It is at first small—about the half of a walnut—and is movable in about one-half of the cases. As a rule, palpation causes no pain at first, though it may prove tender when directly pressed upon.

Dull pain in the lumbar region, suggesting lumbago, may be the initial symptom. This pain gradually increases and, after being centered in the region of the growth, with a sensation of weight, increasingly radiates in various directions, the back, the abdomen and the testicles. It may come on suddenly and last three or four hours, then be followed by hematuria and frequent urination, followed by a period of rest, during which the urine is slightly albuminous. The urine sometimes contains a few casts, oxalate of lime and a few corpuscles. During this period of rest a certain stiffness may be experienced on the side of the tumor. Varicocele is frequently observed in these cases, on the same side as the focus of pain; it may develop simultaneously with the latter and disappear when the patient assumes the recumbent position.

While periodical hematuria, a tumor and pain in the locations mentioned are typical signs of renal hypernephroma,

other phenomena may appear gradually as the morbid process advances. Most important among these are the metastases, which occasionally occur as first signs of the disease. This is especially the case in bone metastasis, which may appear in the vertebræ, the ribs and other long bones, the skull, scapula, etc., *i.e.*, practically any portion of the skeleton. Metastasis may also occur in various viscera, particularly the lungs, the consolidation in the latter suggesting the corresponding stage of phthisis.

Case in which the symptoms and the local findings were so obscure that it was impossible to make a correct diagnosis. The abdomen was opened on the left border of the left rectus muscle. The capsule of the tumor was carefully incised and the peritoneum thus liberated was sewed to the parietal peritoneum of the laparotomy wound, thus shutting off completely the peritoneal cavity from the field of operation. The tumor and the kidney, to which it was attached, were delivered through the incision and the tumor carefully enucleated. No large blood-vessels were severed, but the oozing from the cut surface of the cortex of the kidney could only be arrested by bringing the capsule on one side against the capsule on the other by three mattress stitches. The kidney was allowed to fall back into its normal position. With the exception of the development of a periappendicular abscess in an old appendicitis scar, the patient made an uneventful and rapid recovery. A microscopic examination of the tumor showed that it was a typical adrenal growth. Bayard Holmes (Med. Standard, Nov., 1904).

Series of 27 cases in which a single bone metastasis was the first symptom of the disease. Two were autopsy cases. In one case the metastasis to the scapula was excised, and the patient has remained well so far, eighteen months after operation. In another instance the metastatic area in the occipital bone showed ossification. This so-called osteoplastic carcinosis has been described by von Recklinghausen in metastatic bone foci from carcinoma. Albrecht (Zentralbl. f. Chir., Bd. xxxii, S. 112, 1905).

Case of renal hypernephroma in which the first evidence was a metastasis in the upper part of the humerus, the only sign of the primary growth being an enlargement of the left kidney. Fifteen cases from literature suggested the following deductions in this connection: 1. A bone metastasis may be the first sign of hypernephroma. 2. A bone tumor in a middle-aged or elderly person should suggest a metastatic hypernephroma, for a primary bone tumor in elderly people is uncommon. 3. The bone metastasis from a hypernephroma may be the only metastasis. 4. A hypernephroma may exist for a considerable period without symptoms. 5. The kidney region should be palpated with great care in every case of bone tumor. C. L. Scudder (Annals of Surg., Dec., 1906).

The arteries may be thickened and show clearly defined signs of arteriosclerosis, quite in contrast, sometimes, with the relative youth of the patient, and the blood-pressure be quite high. The skin is not bronzed in these cases, but yellowish, and sometimes swarthy or smoky, this being replaced by pallor when the end is near. The temperature may be raised, but this rarely exceeds 1° or 2° F.

[An important feature in this connection is that bronzing is a characteristic of *insufficiency* of the adrenals, as in Addison's disease, whether due to degeneration, tuberculosis, or malignant tumor of these organs or of their nerve supply. In hypernephroma, on the contrary, we have an addition of adrenal substance to the circulation through the secretory activity of the adrenal rests, as shown by the familiar results of adrenal overactivity enumerated

—high blood-pressure and arteriosclerosis. The icterus or swarthiness here is due, from my viewpoint, to the continuously high blood-pressure which causes the cutaneous capillaries to become hyperemic and to expose an increased quantity of the adrenal principle—the component of melanin (see "Internal Secretions," vol. ii, p. 835) to oxidation. The stage of bronzing is not reached because the pigment is not deposited in the cutaneous tissues, as it is in Addison's disease, but merely supplied to them in excess. C. E. DE M. S.]

The duration of the disease varies from fifteen weeks to eight years. The patient gradually loses flesh and grows weaker, all the symptoms become aggravated, hematuria becoming prominent, causing marked secondary anemia; moderate edema of the lower limbs may appear mainly as a result of pressure on some large venous trunk, and delirium sometimes precedes the terminal coma.

DIAGNOSIS.—The pain in the region of the affected kidney, the hematuria accompanied by frequent urination and the localized tumor, are the chief diagnostic points among those previously enumerated, but other features may serve to facilitate the diagnosis. Gellé pointed out that fragments of the tumor, which is very friable and often dissociated during hemorrhages, could be found in the clots passed with the urine. The cells preserve their characters and staining properties.

As to diagnosis of the tumor itself after removal, Croftan found (1) that a watery extract of fresh hypernephroma, in keeping with adrenalin and adrenal extracts, provoked glycosuria when injected in the rabbit; (2) that a pure starch solution, to which the watery extract of hypernephroma was added, contained an appreciable quantity of dextrose; and (3) that the watery extract also possesses the power to decolorize an iodine starch solution. These simple tests make it possible to differentiate hypernephroma from other tumors of the kidney. This is important, since the post-operative prognosis of hypernephroma is much more favorable than that of any other malignant tumor of the kidney. A high blood-pressure tends greatly to insure the diagnosis.

Hypernephroma can be recognized by the histological structure of the organ, the presence of oil globules in the cells, and the peculiar staining reaction discovered by Lubarsch. Case of a man of 29 years, who died with symptoms of brain tumor, and in whom masses of adrenal tissue were found in the kidney and liver. A careful study of the literature showed that hypernephroma is more common than is usually supposed. Radasch (Amer. Jour. Med. Sci., Aug., 1902).

There are no pathognomonic signs of renal hypernephroma. A diagnosis, especially in the early stages, must be made by a process of exclusion. Two personal cases, one of which was a boy of 14, showed extensive arteriosclerosis. This suggests again the importance of blood-pressure determinations in all cases where a suspected kidney lesion exists. Hematuria is the most important early sign. Metastasis occurred in three instances as late manifestations. Only two of the eight cases were operated upon. They have remained well seven and fifteen months respectively. H. C. Moffitt (Boston Med. and Surg. Jour., Oct. 8, 1908).

A question in regard to these cases which has never been thoroughly investigated is that of increased arterial tension. It is logical to suppose that, with an increase of adrenal tissue, we may have an excess of adrenal secretion, which would result in a rise of blood-pressure—certain writers have noted that this was true; but observations upon this point sufficient to settle the question have not yet been made. Every case of hypernephroma should be thoroughly investigated in

this regard, and we may find that a study of the blood-pressure furnishes us a valuable aid in diagnosis. George E. Beilby (Albany Med. Annals, Jan., 1909).

Various disorders may be suggested by hypernephroma, prominent among which is *urinary calculus*. In this connection the pain is coincident with the hemorrhage, while in hypernephroma the pain continues after the latter, though greatly relieved. The vermicular and cylindrical shape of the clots in hypernephroma is also suggestive. Cystoscopic examination at this time often reveals these clots projecting from the ureter of the diseased kidney, whose tumor can also, in some instances, be discerned under X-ray examination. *Pregnancy* is sometimes suggested when the growth projects anteriorly, especially in view of the fact that amenorrhea sometimes precedes the abdominal enlargement.

Hypernephroma may be mistaken for *enlarged spleen*. The latter is usually nearer the surface and its mobility on inspiration more marked. It is located on the left side, whereas hypernephroma, in most instances, occurs on the right side. Catheterization of the ureters may serve to indicate, between the periods of hematuria, which of the two kidneys is most impaired functionally. The blood count affords little, if any, information, any diminution of red corpuscles—sometimes to an extreme degree—being readily accounted for by hematuria. Moderate leucocytosis occurs in some cases, but not with sufficient frequency to give this sign any diagnostic importance.

In some cases the symptoms and physical signs, other than hematuria, afford but little help to establish the identity of the tumor, either anteriorly or posteriorly. In that case the absence of pregnancy being clearly established, an exploratory incision followed immediately, if hypernephroma be present, by its radical removal, is indicated.

PATHOLOGY.—Hypernephroma is usually located in the upper pole of the kidney, immediately, therefore, under the adrenals. When found early in life at autopsies hypernephromata may be no larger than lentils, or even smaller, but they may attain the size of a child's head, growing outwardly, or, in some cases, inwardly, at the expense of the renal tissues. They reproduce more or less perfectly, the adrenal tissue, the smaller growths being made up, as a rule, of the cortex, and the larger of both the cortical and the medullary substance. They are firm when small, but when they attain a certain size their tendency is to become lobulated, the projecting masses becoming softer and cyst-like. They are lobulated owing to the fibrous bands derived from the renal capsule, and the lobules, when opened, may be yellowish, grayish red, or brown or blackish, and contain hemorrhagic areas—the source of the blood which causes hematuria.

[The various colors mentioned correspond suggestively with the cutaneous pigments I have ascribed to the adrenal principle in icterus bronzing, etc., and this, in turn, further confirms the fact that the melanins are mainly composed of this principle ("Internal Secretions," vol. ii, p. 835). Hence the association of hypernephroma with melanotic sarcoma by various pathologists. C. E. DE M. S.]

The larger growths are those which tend to become malignant and to produce metastases. These occur through the blood-vessels, both the arteries and veins; the bones and lungs, as previously stated, are the structures most frequently invaded, though, occasionally, extension occurs by the lymphatics, including the retroperitoneal glands.

Microscopically they usually contain a scanty stroma composed of vascularized connective tissue in columns and a parenchyma formed of endothelial polygonal or columnar, translucent nucleated cells, which differ entirely from those of the renal epithelium. The cytoplasm is granular and contains, besides detritus and giant cells, numerous fat-laden vacuoles. It is the presence of considerable fat which first caused these tumors to be regarded as lipomata. The fat contains lecithin. Glycogen is also present, sometimes in relatively large quantities.

Prior to 1883 many forms of renal growths were grouped under the head of lipomata. Some authors had previously, and others since that time, described these neoplasms as adenomata arising from the renal tissue itself. Grawitz was the first to bring order out of chaos when he maintained that these growths formerly described as lipomata in reality had their origin in suprarenal tissue misplaced within the kidney. His reasons for believing these tumors to be of adrenal origin were: (1) the subcapsular position in which aberrant adrenal tissue is likely to occur; (2) the cells were quite different in form from the renal cells, and contained fat-globules in large drops like fatty infiltrated liver-cells; (3) the capsule and the arrangement of the tumor-cells in rows, like the suprarenal cortex, the preponderance of cells over stroma; (4) amyloid degeneration of blood-vessels present in his case only in the adrenals. Others, like Chiari, Lubarsch, and many others, supported Grawitz's views and added the following criteria: (1) the similarity between tumors of the adrenal body itself and these growths; (2) the presence of glycogen. The frequency with which portions of the suprarenal tissue are found under the true renal capsule and imbedded in the renal cortex was shown to be astonishingly great by Grawitz. L. L. McArthur and D. N. Eisendrath (Phila. Med. Jour., April 29, 1899).

Four personal cases illustrating the stages of transition from the smallest benign neoplasm, a pure aberrant adrenal germ to the large growth which assumes the characteristics of a cancer.

Gradually as the malignant growth is approached, the adrenal germs or "rests" lose their normal characters to assume the vague embryonic cellular types. These correspond in every way with the renal cancers containing translucent cells which certain classic writers still consider as renal cancers, but which in reality are hypernephromata. E. Gellé (L'Echo méd. du Nord, Aug. 2, 1908).

PROGNOSIS.—As a rule, hypernephromata grow slowly at first, months, and even years, elapsing before they metastasize or show other signs of malignancy. They may then progress very rapidly, and, the hematuria becoming continuous, death occurs from exhaustion.

A case was reported by Hausemann in a woman 60 years of age, in whom the tumor had been present fifteen years without evidence of rapid growth. Suddenly the tumor began to grow rapidly and the hematuria which until then had been periodical and not profuse, became continuous. The patient died of exhaustion within a few months. Kusmik (Beiträge zur klin. Chir., Bd. xlv, S. 185, 1905).

They show a tendency to recur, though years may elapse before recurrence occurs. If recognized early, however, removal affords a greater chance of permanent recovery.

Out of 4 cases, 1 of the patients already reported was known to be well seven months after operation; another has remained well fifteen months, but the presence of a varicocele on the sound side renders his future doubtful. Dr. Levison operated on a second case that remained well for some years. Out of 24 cases with operation recorded by Albrecht, 8 died from the immediate results of the procedure and 9 soon

afterward from local recurrence or metastases; 1 died of pneumonia two years after operation, and autopsy gave no evidence of recurrence. Only 4 patients remained well after three years, and of these 1 developed metastasis in the occipital bone at the end of four years; a second, metastasis in the scapula after four years and three months; a third, metastasis in the spine after seven years. Only 1 patient out of the 24 remains well after four years. The danger of metastases years after operation renders prognosis most uncertain. Claimont has recorded a case of recurrence in the bronchial glands ten years after removal of a renal hypernephroma. It must be remembered, however, that Albrecht has shown that there may be but one metastasis, and removal of this may lead to a permanent cure. The disheartening results of operations in the past should spur on the clinician to try all methods that may lead to early recognition of the growths. H. C. Moffitt (Boston Med. and Surg. Jour., Oct. 8, 1908).

TREATMENT. — An **exploratory incision** is warranted, as previously stated, when an abnormal growth in the abdomen or in the region of the kidney occurs coincidently with hemorrhage, even when other symptoms of hypernephroma are not present. The majority of authorities consider this procedure advisable even when hemorrhage into the bladder cannot be accounted for. In some cases discomfort or tension over one kidney, and deep comparative palpation on both sides may suggest which side should be explored first; but if this unilateral examination fails to indicate the presence of a growth, exploration of the other kidney is justifiable. In some instances the organ is merely enlarged, especially toward the upper pole, or at the hilum. **Removal** of the growth may be performed extraperitoneally through a lumbar incision. The fatty capsule should, according to Kuzmik, be removed along with the growth, as it may be infiltrated and thus lead to recurrence.

Case in a woman aged 37, married, who had an abdominal swelling the size of a fetal head at term. It was very mobile and fluctuant, and could not be pushed down into the pelvis. A diagnosis of cyst of the kidney or ovarian cyst with a long pedicle was made. On opening the abdomen the tumor was found to be retroperitoneal and crossed by the descending colon. The peritoneum was divided and the cyst enucleated. There was no pedicle. The cyst lay immediately in front of the left kidney, which was normal. The patient made a rapid recovery. On section the tumor contained blood and clots. The cyst-wall showed fibrous septa inclosing polyhedral granular nucleated cells, closely resembling the "zona glomerulosa" of the normal suprarenal capsule. Archibald Donald (Brit. Med. Jour., Dec. 9, 1899).

Two cases of hypernephroma, both of which were absolutely well one year after operation, a **nephrectomy** having been done at that time. Keen, Pfahler and Ellis (Amer. Med., Dec. 17, 1904).

An extraperitoneal operation can be done even for the removal of a very large tumor, although it is possible only when the tumor has slowly grown into the tissues of the mesocolon, and the ventral or right peritoneal surface of the colon has become greatly hypertrophied or enlarged, and the blood-vessels of the colon so distorted that a long incision would not, in any way, vitiate the blood-supply of this large duct. The results of a personal operation also showed the necessity of taking advantage of every opportunity to completely remove a neoplasm, no matter how grave the prognosis may be at the time of operation. Bayard Holmes (Med. Standard, Nov., 1904).

Case of hypernephroma of the left kidney in which the following proved successful: the patient having been

perfectly well fifteen months before the present report. A Morris incision on the left side began about 2 cm. outside the quadratus lumborum and extended forward and downward to the level of the anterior superior spine. This necessitated division of the external oblique muscle. The peritoneum was pushed forward and the kidney tumor removed after much difficult dissection. The tumor and kidney measured 18 x 10 x 8 cm., and was densely adherent at the upper border. The vessels were ligated high up, and on account of the high position of the tumor the tips of the tenth and eleventh ribs were divided subperiosteally and the diaphragm raised with retractors. Most of the capsule was removed and the ureter was stripped downward, almost to the bladder, and cut short after carbolizing the end. The vessels were large, but not occluded by the tumor mass, and were ligated by Pagenstecher. The peritoneum was opened at the upper end of the incision, but was easily closed with continuous catgut sutures. The hemorrhage was fairly severe from the capsule, but was readily controlled. The remnant of the capsule was stitched with catgut and a cigarette drain inserted in the space. Muscles sutured with chromicized gut, skin with silkworm gut and continuous plain catgut. Sterile gauze dressing. H. C. Moffitt Boston Med. and Surg. Jour., Oct. 8, 1908).

C. E. DE M. SAJOUS,
Philadelphia.

ADRIN. See ANIMAL EXTRACTS: ADRENALS.

AGALACTIA. See MAMMARY GLAND.

AGAR-AGAR is the East Indian name of a substance extracted from various seaweeds, which is available in the shops in the form of long, transparent strips resembling goose-quill pith, and also in quadrangular cakes weighing about 150 grains (10 Gm.) each. It consists chiefly of gelose, and is soluble in hot water, though insoluble in cold water. It has been extensively used as a culture medium and as a demulcent, combined with glycerin for chapped hands and lips.

Recently, however, it has been used for constipation in doses ranging from 1½ drams (6 Gm.) to ½ ounce (8 Gm.), coarsely comminuted and mixed with food. It becomes a jelly in the stomach and intestines by absorbing water and, being indigestible, gives considerable bulk to the feces, thus promoting defecation mechanically. A. Schmidt gives agar-agar cut up in small pieces, adding 25 per cent. of an aqueous extract of cascara sagrada. One teaspoonful to a tablespoonful in mashed potatoes or any other soft food is given daily in chronic constipation. S.

AGARICIN is obtained from the white agaric (*Boletus laricis*), a fungus growing on the trunk of the European larch. The activity of agaricin is due to agaricic, agaricinic, or agaric acid. The pure acid occurs as a white, silky powder made up of minute prismatic or lamellar crystals, and having a bitter taste. It is soluble in alcohol, and in hot water, and but slightly so in cold water, ether, and acetic acid. It forms soluble salts with the alkali metals. *Agaricic acid* is the preparation from agaric generally used in therapeutics under the name of agaricin. The commercial agaricin, on the other hand, is an impure resinous product obtained by extraction from the crude drug, and is much weaker in its effects than the acid.

DOSE.—The dose of *agaricic acid* is 1/15 to ½ grain (0.004 to 0.03 Gm.). It is usually given in pill form, but may also be administered hypodermically, when the dose should be one-half smaller. The *resinous agaricin* is sometimes used, the dose being from 1 to 5 grains (0.065 to 0.3 Gm.). The doses given should at first be small; they can then gradually be increased as the patient becomes partially tolerant to the effects of the drug.

PHYSIOLOGICAL ACTION.—Agaricic acid in therapeutic doses decreases markedly the activity of the sweat-glands. It probably acts on the secretory nerve-endings to these glands (Hofmeister), thus resembling atropine in its action. It exerts, however, no inhibiting influence on

the other secretions of the body, including the salivary secretion, and does not affect the pupils. In larger doses it causes purging and sometimes vomiting by an irritating effect on the gastrointestinal tract. No serious constitutional results are ever produced by it when used internally because of the slowness with which it is absorbed. It has no cumulative action. Toxic effects from it may be observed, however, upon its intravenous injection in large doses into animals, and less readily upon subcutaneous injection. It excites primarily, and secondarily causes, progressive paralysis of the bulbar centers, including the vagal and vasomotor centers. The animal shows marked weakness, becomes dyspneic, has convulsions, and dies as a result of paralysis of the respiratory center. Subcutaneous injections of agaricic acid produce inflammation of the surrounding tissues, sometimes followed by abscess formation. When applied to abraded areas or to mucous membranes it acts as a local irritant.

THERAPEUTICS.—Agaricin (agaricic acid) is of great value in the treatment of the **night-sweats** of pulmonary tuberculosis. Doses of 1/6 to 1/2 grain (0.01 to 0.03 Gm.) are generally effective; according to Conkling, 1/12 grain (0.005 Gm.) will often suffice. Where the gastric digestion is good, it is well tolerated, and often causes diminution or even complete disappearance of the sweats (Andral, Legougeux), especially in the second and third stages of the disease (Combemale). The action begins two hours or more after administration, and reaches its height three hours later. Taken before retiring, agaricin will sometimes prevent the occurrence of a night-sweat, thereby relieving the patient from the consequent exhaustion.

While not as certain a remedy as atropine, it is advantageous in not causing the other unpleasant effects of the latter, such as drying of the mouth and fauces, nausea, and dilated pupils. It may be given in combination with aromatic sulphuric acid, which has a similar action in reducing sweats. Where agaricin is found to cause gastrointestinal irritation and a tendency to diarrhea, it is sometimes prescribed with small amounts of some preparation of opium,—Dover's powder, for example.

Agaricin is used to counteract **excessive sweating** from other causes than phthisis, including various infections and intoxication by certain drugs (coal-tar antipyretics, salicylates). It has also been employed **to arrest the secretion of milk.** Its action can be kept up, if desired, by giving small doses repeatedly. S.

AGGLUTINATION TEST.

—This test, also known as the **Widal reaction** or the **Gruber-Widal reaction,** is used to establish the presence of typhoid fever. It is based upon the fact that in this disease the specific bacteria in free dilution "agglutinate," that is to say, adhere to one another and lose their motile power, thus forming clumps or masses in the solution examined.

The essential feature of this test is that, while normal serum, *i.e.,* the serum of a normal individual, when diluted up to a certain limit, will agglutinate many bacteria besides the typhoid bacillus, the latter organism causes the production of so great a quantity of the substance "agglutinin," which provokes the phenomenon, that, even when a drop of serum from a typhoid patient is diluted 50 times or more with saline solution, agglutination of typhoid bacteria, obtained from a recent culture of these germs, will occur. The reaction is only reliable, in fact, when the degree of dilution is not below 1 to 50.

The *microscopic* reaction requires a slide with a concave depression in the middle of one of its surfaces. A small quantity of the patient's serum is obtained by pricking the ear or the finger. This quantity is diluted in fifty times its volume of saline solution. A drop of this is then placed on a cover-glass, with a drop or loopful of fresh bouillon of genuine typhoid bacilli. The cover-glass is then inverted and placed over the concavity of the slide in such a way as to cause the mixture to hang downward. Hence the term "hanging drop" method. The edges of the cover-glass being then sealed with paraffin or vaselin, the slide is examined under the microscope, using the one-twelfth oil-immersion lens, and the clamping and loss of motility of the typhoid bacilli ascertained. If more than 4 bac-

teria are permanently agglutinated, the test is positive.

This method is only applicable, however, in hospitals, where a clinical microscope is available, unless the physician carries his microscope to the patient's home. This inconvenience can be readily obviated, however, by dipping a piece of absorbent paper in the patient's blood. When dried this paper can be used for the test by placing it in forty to fifty times the quantity of saline solution that the paper contains of serum. The latter will then dissolve in the saline solution, and a drop of the mixture with the drop of typhoid bacilli culture can then be used as described above.

Or again, "3 drops of blood are taken from the well-washed aseptic finger-tip or lobe of the ear, and each lies by itself on a sterile slide, passed through a flame and cooled just before use; this slide may be wrapped in cotton and transported for examination at the laboratory. Here one drop is mixed with a large drop of sterile water to redissolve it. A drop from the summit of this is then mixed with 6 drops of fresh broth culture of the bacillus (not over twenty-four hours old) on a sterile slide. From this a small drop of mingled culture and blood is placed in the middle of a sterile cover-glass, and this is inverted over a sterile hollow ground slide and examined. A positive reaction is obtained when all the bacilli present gather in one or two masses or clumps and cease their rapid movement inside of twenty minutes" (Green-Hughes).

The test may also be carried out without the aid of a microscope; this is the *macroscopic reaction*. Several bouillon cultures being available, 5 c.c. of each culture are placed in as many test-tubes as there are cultures. To each test-tube is then added sufficient serum of the suspected case to obtain a solution of 1 to 50. The test-tubes are then kept at blood or room temperature from three to seven hours. Their contents will then have become clearer, the bacilli having been precipitated to the bottom of each test-tube if the reaction is positive. It is obvious, however, that the microscopic reaction is preferable and less liable to mislead.

That the value of the Widal reaction is very great is now generally recognized. Kneass and Stengel in statistics based on over 2000 cases give 95.2 per cent. as the proportion in which true cases of typhoid fever had given a positive reaction, while no reaction occurred in 98 per cent. of the cases which eventually did not prove to be typhoid. Abbott, in statistics based on 4154 cases for which the Widal reaction was taken in the municipal laboratories of Philadelphia, places at only 2.8 per cent. the possibility of error. S.

AGORAPHOBIA. See INDEX.

AGURIN, a diuretic, is a double salt of theobromine sodium and sodium acetate, which contains 60 per cent. of theobromine. It occurs in the form of a fine crystalline powder, which is freely soluble in water, and but slightly so in cold alcohol.

MODES OF ADMINISTRATION.—Agurin is hydroscopic and, in aqueous solution, readily splits into its components. Hence, the advisability of prescribing it in capsules or in tablets, 5-grain tablets being available in the shops. The dose is from 5 to 10 grains (0.3 to 0.6 Gm.) three to five times a day. It is also absorbed from the rectum when given in an enema of plain water.

THERAPEUTICS.—Agurin is especially efficacious as a diuretic in cardiac dropsy and acts well in combination with digitalis. It acts like theobromine (*q. v.*) and is, unlike diuretin, well borne by the stomach. It also gives good results in **interstitial nephritis**, especially when combined with the milk diet. This applies also to **hepatic cirrhosis**, though to a less marked degree. Agurin presents the advantage of promoting diuresis without increasing the blood-pressure, a property which renders it particularly useful in cases of **dropsy of cardiac, renal, or hepatic origin** in which arteriosclerosis renders diuretics which raise the blood-pressure dangerous. S.

AINHUM. —African word meaning "to saw off."

DEFINITION.—Ainhum is a disease occurring exclusively in negroes and consisting in the spontaneous amputation of the little toe by an adventitious fibrous band.

SYMPTOMS.—The first indication of the disease is a furrow on the lower surface of the little toe, and occasionally other toes, at the proximal interphalangeal joint. This furrow, the result of the circumferential pressure exerted by a fibrous ring, gradually deepens until the bone is reached, this process taking several years, sometimes as many as ten. The distal portion of the toe becomes greatly hypertrophied, then finally drops off, the stump healing without further complications in the great majority of cases. It does not give rise to much suffering, owing to its very gradual progress. It is sometimes mistaken for leprosy. It has been observed in the white race also.

Though rare in the United States, ainhum is so common in India that Crawford found a case in every two thousand surgical patients in Indian hospitals. The absence of pain or inconvenience in many cases also probably prevents their being reported. The ultimate result of the disease, which begins as a crack or fissure, is the spontaneous amputation of one or more fingers or toes by a gradual circular strangulation. In the writer's case, complete amputation of one toe and partial amputation of another had occurred before the patient sought medical assistance or appreciated his condition. It is rare in females, and is almost exclusively confined to the dark-skinned races, only 4 cases having been reported in whites. It is probably a trophoneurosis of unknown origin. N. D. Brayton (Jour. Amer. Med. Assoc., July 8, 1905).

Case of ainhum in a white girl in Florida. The case is of interest because of the appearance of ainhum in the Southern States and heretofore reported in the negro race only. When ulceration takes place the ulcer assumes a resemblance of a necrotic ulcer with a distinct nauseous color. As advanced by Unna, the condition is a sclerodermic callosity, with ring formation, producing a stagnating necrosis. The tumefaction indicates a stagnation, resulting in degeneration, retraction, and finally disappearance of the phalanges. The disease sometimes covers a period of several years. Eskridge (Med. Rec., Sept. 17, 1910).

Two cases of ainhum that the writer has cared for at Garfield Hospital Dispensary. He watched the progress of the case for two years, and showed photographs and skiagraphs of them, taken at the beginning and end of observation. One case, in a negress, a native of Maryland, was of sixteen years' duration, but only slightly advanced. The pain in the crack was, however, sufficient to induce her to have the toe amputated. The specimen showed the groove in the soft tissues and the slight atrophy of bone.

The other case, also in a negress, a native of Georgia who had lived fifteen years in the District of Columbia, was of about twenty-five years' duration and much more marked than the other case; the groove around the toe was deepest on the plantar and inner margins of the toe and had penetrated almost to the toe-nail. The middle phalanx was practically gone; only the nail-bearing part of the ungual phalanx remained; the basal phalanx was atrophied about one-half. The advance of absorption of bone was quite plain in the skiagraphs. The skin of the feet and hands showed a scaly condition. As the toe had given but little pain, the patient declined to have it amputated, and was therefore presented herself. Truman Abbe (Washington Med. Annals, Nov., 1910).

ETIOLOGY.—Ainhum is always observed in negroes, especially of the western coasts of Africa and South America. A number of cases have also been reported in the United States by Bringier. Hindoos are said to also suffer from the disease. Self-mutilation has been suggested by some observers, but the likelihood of this cause is very slight. Heredity does not seem to play any rôle in its production.

PATHOLOGY.—The lesions observed have been hypertrophic thickening and

retraction of the derma, with consequent atrophy of the underlying bone (Hermann, Weber, Wucherer, Schüppel). It has been confounded with congenital amputation, but, as stated, ainhum is never congenital. That the disease bears some connection with leprosy is insisted upon by some authorities. According to Zambaco Pacha, undoubted symptoms of leprosy are present in all cases of true ainhum. It should be looked upon as an attenuated form of the latter disease. Its relations to scleroderma are explained by the fact that this latter affection is a special form of leprosy. It has also been attributed to syphilis, larvæ, and atavism.

The writer agrees with Matas in terming ainhum a trophoneurosis. Personal case in a negress of 65 years whose right little toe was affected in the characteristic way. The toe was disarticulated at the metatarsophalangeal joint under cocaine anesthesia, and the cicatrix has since remained in healthy condition. H. N. Blum (Med. Record, Oct. 22, 1904).

No definite and undisputed cause for the lesion has yet been proved, but the writer thinks that there is most to be said in favor of de Silva Lima's view that it is due to traumatism. The splay-footed negro is especially liable to such, and the groove around the toe in this disease, both macroscopically and histologically, is a cicatrix. The later fatty and atrophic conditions in the amputated toe are not yet fully explained, but may depend on local cicatricial formations or may be of trophic origin. Wellman (Jour. Amer. Med. Assoc., March 3, 1906).

TREATMENT. — Surgical measures alone prove of value in these cases. Early **section** of the fibrous ring is sometimes sufficient to arrest the progress of the disease, or **division of the skin** down to the periosteum on the opposite side of the seat of the disease may be resorted to.

Murray successfully treated a case by dividing the skin and all the tissues down to the periosteum, on the side opposite to the seat of the disease. S.

AIROL, or bismuth oxyiodogallate [C_6H_2 $(OH)_3$. COO. BiOH], is a compound of gallic acid and bismuth subiodide. It occurs in the form of a bulky, grayish-green powder, devoid of odor or taste. It is insoluble in water, alcohol, chloroform, and ether, but is slightly soluble in glycerin and is dissolved in alkaline solutions and dilute mineral acids. When exposed to moisture, including wound secretions, it is gradually changed into a reddish powder, due to the liberation of a portion of its iodine: this change occurs with great rapidity when boiling water is applied to airol.

MODES OF ADMINISTRATION.— Internally airol has sometimes been given in doses of 2 to 5 grains (0.13 to 0.32 Gm.). Externally it is used principally in the powder form, which is dusted over the surface involved after it has been washed with hydrogen peroxide or other cleansing agent. It may also be applied in an ointment containing about 2 to 4 drams of airol to the ounce of petrolatum, or in a 10 per cent. glycerin emulsion containing equal parts of glycerin and water. The latter preparation may be injected in septic areas. In the treatment of skin lesions it has been applied as a paste containing 2 parts each of glycerin and mucilage to 1 part of airol, mixed with a sufficient amount of refined clay or kaolin (Brun's paste). Airol has also been used as a vaginal suppository. An airolated gauze (20 per cent.), similar to iodoform gauze, is frequently employed. The fact that this substance is decomposed by free contact with water should always be kept in mind.

PHYSIOLOGICAL ACTION. — When used internally or by injection in large amounts, airol has been known to cause symptoms similar to those of bismuth poisoning. Thus Semmer witnessed a case in which 55 grains of airol as a 10 per cent. solution in olive oil injected into an abscess, resulted within three days in softening of the gums, darkening of the buccal mucous membrane, foul breath, headache, nausea, and prostration. Marked irritative effects have also been observed (Zelemsky, Goldfarb), though a total amount of 15 grains taken within three days was found by Haegler to cause no unpleasant effects.

THERAPEUTICS.—Airol is valuable externally as an **antiseptic,** astringent, desic-

cant, and protective. Its germicidal properties are mainly due to the liberation of iodine upon exposure to moisture.

Haegler considers airol the equal of iodoform in disinfecting power, and it has the added advantage of being without odor. It is frequently used as an antiseptic dressing for open wounds, including **surgical wounds**, and generally causes no pain when applied. It has been applied to **infected ulcers** of different kinds, **varicose ulcers** (Fahm), **burns** of the second degree, and to the lesions of various skin diseases, such as **intertrigo** (de Sanctis), etc. It has proven useful when injected with glycerin in **abscesses** of pyogenic or primarily tuberculous origin.

In **ulcerations of the cornea**, airol has been applied in powder form with success (Gallemaerts, Bonivento).

Airol has been used for the treatment of **uterine** and **vaginal inflammations.** It may be incorporated in the usual cocoa-butter suppositories for vaginal use, or introduced into the uterus and vagina on gauze moistened with a liquid mixture. Delbert dips a wick of aseptic gauze in a 1 to 4 emulsion of airol in glycerin and inserts it through the previously dilated cervix into the uterine cavity; he then packs the vagina with tampons of absorbent cotton dipped in a 1 to 20 emulsion, and does not remove it for forty-eight hours (Manquat).

Airol may be given where an astringent effect on the intestinal tract is desired. Fahm has recommended its use in **tuberculous enteritis.** S.

ALBARGIN, or gelatose silver, an antiseptic and germicide, is a compound of silver nitrate 15 parts and gelatose 85 parts. It occurs as a light, brownish-yellow, shining powder, which is freely soluble in equal parts of both cold and hot water, making a permanent solution if not exposed to light. It is incompatible with ferric and ferrous chlorides, tannin, opium, resins, and the essential oils.

THERAPEUTICS.—Albargin is mainly used as a substitute for silver nitrate in the treatment of **gonorrhea.** Its aqueous solutions being neutral, it may be used as injections in strengths from ½ to 2 per cent. Its molecule being smaller than that of albuminous preparations of silver, it is thought to penetrate more thoroughly and promptly the diseased tissue and destroy the gonococci therein. Albargin has also been found efficacious in the treatment of **chancroids.** Its use is painless, and it does not irritate mucous membranes; it may safely be used, therefore, in the treatment of **gonorrheal ophthalmia.** S.

ALBUMINURIA. — DEFINITION.—The presence of albumin in the urine, a condition now known to occur under many circumstances without necessarily indicating the presence of serious morbid changes in the kidney.

Albuminuria may be *true*—when the albumin is dissolved in the urine—or *spurious,* when caused by admixture of semen, pus, or blood in the urine. Spurious albuminuria is easily distinguished from the true form by the aid of the microscope. Both kinds of albuminuria may occur simultaneously.

Domenico Cotugno discovered, in 1770, that urine may contain albumin; by boiling a sample of urine he found that pure albumin was precipitated. It was long maintained by all authors that albuminuria was always a symptom of disease, but of late many authorities have admitted that albuminuria may be compatible with perfect health.

Posner maintains that albumin is always found in the urine, but normally in too small quantity to be revealed by the ordinary reagents. To demonstrate the presence of albumin in normal urine Posner evaporated large quantities of urine at low temperature and tried the different reagents in the concentrated urine. His experiences were repeated and his views supported by Senator and by Leube, who, however, did not

find albumin in all cases. Von Noorden, Winternitz, Lecorché, Talamon, and other authors do not admit that albumin is a constituent of the normal urine; but this was recently denied by Mörner, who found that it invariably contained at least 22.78 mg. (about 3.5 of a minim) per liter.

Different kinds of albumin may be present in the urine; generally the proteids contained in the blood-serum are to be found,—viz.: (1) the serum-albumin, and (2) the globulin, or paraglobulin; in most cases both these proteids are present, but in varying proportions. In some cases there may also be found (3) hemialbumose, or propeptone, a mixture of different albumoses which are not precipitated by boiling; (4) nucleoalbumin, which has also erroneously been called "mucin," and (5) peptone. Joachim found pseudoglobulin in every case of albuminuria, while euglobulin was often absent. The albumin content mostly exceeds that of the globulin.

The writer carefully estimated the amount of serum-albumin, of euglobulin, and of pseudoglobulin in various forms of albuminuria, by means of fractional precipitation with sulphate of ammonia, and subsequent determination of nitrogen by Kjeldahl's method. Euglobulin was never found in febrile albuminuria. The globulinic index cannot be accepted as a guide in the discrimination of various kinds of albuminuria, as it varies in such wide limits in cases which are closely akin to each other. No reliance can be placed on the albuminoid index as a prognostic criterion, for, although sometimes it was higher in cases where the kidneys were comparatively free from disease, the reverse was the case at other times. The author did not find a marked increase in globulin in acute nephritis, febrile albuminuria, orthostatic albuminuria, and the albuminuria of pregnancy. Balocco (Gazz. deg. Osped., Jan. 28, 1906).

The urine may, of course, also contain albumin in connection with hematuria and hemoglobinuria, but such cases cannot be classed as true albuminuria.

PHYSIOLOGICAL ALBUMINURIA.—Regarding the origin of the albumin in the urine only guesses can be made; two theories are possible: (1) the albumin may come from the glomeruli; (2) from the tubular epithelial cells.

Formerly the opinion predominated that the fluid which escaped from the glomeruli was albuminous, but that the albumin was absorbed during the passage through the healthy renal tubules, diseased tubular epithelium being unable to absorb the albumin. This has not been proved, however, and most modern authors believe that albumin is not contained in the urine coming from the glomeruli, except when these are diseased or when the pressure of blood in the glomeruli is abnormally great. Runeberg, on the contrary, is of the opinion that albuminuria is caused by low pressure of blood, and supports this opinion by experiments with animal membranes, but experiences with dead membranes cannot be regarded as conclusive for the action of the living kidney.

Von Noorden and other authors regard the tubular epithelium as the unique source of albuminuria. These epithelial cells are subject to successive disintegration: when this is minimal, and successive traces, only, of albumin are found in the urine, the albuminuria is physiological; when the disintegration of the tubular epithelial cells is augmented and hastened by disease, a morbid albuminuria takes place. In

his opinion, this theory is supported by the fact that nucleoalbumin, of which the protoplasm of the cells undoubtedly is the source, is always found in normal urine.

Senator considers physiological albuminuria in the same light as physiological glycosuria, and, among the causes that give rise to it in susceptible individuals, he mentions: severe exertion of the lower extremities, eating and digestion of hearty meals, menstruation, cold baths, psychical excitement, etc. He deems albuminuria pathological only when it does not disappear promptly on the cessation of the particular stimulus that caused it. Physiological and allied forms of albuminuria are attributed to congenital predisposition of the individual to disease of any organ which directly or indirectly may influence the elimination of albumin.

> The occurrence of albuminuria is to be regarded as pathological only when it does not take place under unusual conditions alone, and does not disappear promptly on the cessation of the particular stimulus that caused it. Orthostatic albuminuria is distinctly pathological, and most cases of this or cyclical albuminuria are caused by a slight irritation or inflammatory state of the kidneys, which may go on to recovery or may develop into a chronic diffuse nephritis. Physiological and allied forms of albuminuria are based upon congenital or acquired predisposition of the individual, which consists in an abnormality of various organs, such as the kidneys, the digestive tract, the blood-vessels, or the body fluids. Senator (Deut. med. Woch., Dec. 8, 1904).

> Study of the albumin in the urine of normal children. In each specimen of urine, the writers determined the color, the appearance, the specific gravity, the reaction (in twenty-four-hour specimens, the total acidity), the presence or absence of albumin, sugar, acetone, diacetic acid, indican, urobilinogen, and phenol; and microscopically, the presence or absence of cells, casts, cylindroids, and crystals. Four hundred and forty-five specimens of urine were examined. These were obtained from 124 children, ranging in age from 18 months to 14 years. During the period of examination the usual routine of life was followed, except that the children were kept from school. There was no relationship between the specific gravity and the form or amount of albumin. The reaction had no influence on the production of albumin. Sugar, acetone, and diacetic acid were never found. They may, therefore, be considered as having no bearing on the production of albumin. Indican, phenol, and urobilinogen, when present, were usually associated with albumin, but albumin was sometimes absent when they were all present, and the amount was never greater when associated with them than it was in the cases in which they were absent. Crystals, when present in amounts, such as are occasionally found in normal children, are in no way responsible for the associated albumin. The mild disturbances of the intestinal digestion, as shown by the examination of the stools, were not sufficient to account for the occurrence of albumin. The blood-pressure was within the normal range in all cases and, therefore, did not influence the albumin output. The albumin elimination was the same on mixed and exclusive milk diets. They found no children in whom the albumin excretion corresponded to the requirements for postural or orthostatic albuminuria, a rather surprising result in view of the frequency with which this condition is supposed to occur.

> Thirty-two and one-half per cent. of the children showed occasional hyaline casts and cylindroids in the urine. The authors do not consider their "occasional presence" as indicative of a lesion of the kidneys, but rather as suggesting a temporary overtaxation of the kidneys resulting from variations in the habits of life of the individuals, which are too slight to be recognized. Eighty-

eight and seven-tenths per cent. of the urine of these 124 children showed albumin, 27.4 per cent. showed serum-albumin alone and in combination, and 85.4 per cent., an albuminous body precipitated by acetic acid in the cold. These two albumins were nearly always present in very slight traces, occasionally in slight traces, and rarely in traces. In 38 children the twenty-four-hour specimens showed nucleoalbumin in all but 1, and in this case samples examined over prolonged periods of time showed nucleoalbumin frequently. In these 38 children, the percentage of serum-albumin was very much larger (42.1 per cent.) than in the total number of cases examined. The authors believe, therefore, that it is possible to demonstrate in the urine of every presumably healthy child traces of an albuminous body precipitated by acetic acid. Consequently, this substance must be regarded as an exceedingly common, if not constant manifestation in the urine of children under 14 years of age, and as of no clinical significance. The writers do not believe that serum-albumin in the amounts in which it appears in these children indicates a diseased condition of the kidneys any more than does the presence of occasional hyaline casts and cylindroids, and that its etiology may be considered the same as that given for these former elements. Hamill and Blackfan (Amer. Jour. of Dis. of Children, Feb., 1911; Jour. Amer. Med. Assoc., Mar. 4, 1911).

From a pathological point of view the causes of albuminuria may be divided into three groups: 1. Disturbances of circulation. 2. Changes of the tubular epithelial cells or of the walls of the blood-vessels of the kidney. 3. Changes in the composition of the blood.

1. All disorders of circulation capable of causing a venous renal congestion will increase the blood-pressure in the capillaries of the kidney, and thus give rise to a transudation of albuminous liquid; when the congestion is very great the urinary tubules may even be compressed and the escape of the urine rendered difficult. When this is the case and when, also, the supply of arterial blood is diminished, the tubular epithelium will be damaged, and the first result of all this is albuminuria. It is very improbable that arterial congestion ever produces albuminuria, although the experiments of Munk and Senator tend to prove the contrary. Leube found in the early stages of aortic insufficiency, not accompanied by cyanosis, edema, etc., a slight albuminuria. Pathological examination of the kidneys showed the walls of arteries and capillaries much thickened. He makes these changes and their consequences responsible for the malnutrition of the kidney and its result: albuminuria.

A complicating parenchymatous nephritis may exist, as where the endocarditis is caused by diphtheria. The nephritis is generally amenable to treatment, while endocarditis persists. There may be a general atheroma, which also involves the renal vessels, leading to arteriosclerotic kidney. This is especially common with aortic insufficiency. When the energy of the heart sinks and the cardiac muscle undergoes fatty degeneration, stasis, followed by cyanotic induration, is found in all the organs. This occurs only in the later stages of aortic insufficiency. Besides this there is, however, another form of albuminuria, characteristic for the early stages of aortic insufficiency and not accompanied by cyanosis, edema, etc. The urine is not diminished in amount, the specific gravity is relatively low, and the amount of albumin, hyaline and granular casts very slight. Pathological examination of a few kidneys of this kind shows that the marked variations in pressure are responsible for certain anatomical changes. The walls of the arteries and capillaries are found much thickened; so that the amount of blood carried to the kidneys must nec-

essarily be less than normal. The liver and spleen show similar lesions, but never the lungs. V. Leube (Münch. med. Woch., July 28, 1903).

2. Changes of the tubular epithelia and the walls of blood-vessels of the kidneys may, as already stated, be due to disorders of circulation, but they may also be caused by different poisons and toxins. When albuminuria is chiefly caused by degeneration of the tubular epithelia, their protoplasm dissolves in the urine, and nucleoalbumin in great quantity is contained in it, combined with serum-albumin and globulin.

Menge and Schreiber noted albuminuria in several cases in which the kidney had been palpated bimanually, as a result of the circulatory changes produced during the examination. This procedure has been used by Schreiber in the diagnosis of doubtful cases of floating kidney.

Albuminuria following renal palpation. Renal hematuria with albuminuria noted in several cases in which the kidney had been examined bimanually and in which no albumin had been present in the urine before examination. The pressure to which the kidney is exposed causes circulatory changes which permit of the transudation of serum from the renal capillaries. C. Menge (Münch. med. Woch., June 5, 1900).

If a floating kidney be palpated in the usual manner, albumin will almost always appear in the urine, even where only a small portion of the kidney can be grasped between the fingers. The color of the urine voided after palpation is generally somewhat paler, and microscopical examination shows an abundance of epithelial cells from the pelvis, ureter, and bladder, cylindroids, red and white blood-cells, but hardly ever casts.

The albuminuria is very probably caused by the passage of serum from the capillaries into the tubules. Probably some lymph also reaches the latter, since there frequently is no relation between the degree of pressure exerted and the amount of albumin. The observation is of great clinical value, since a doubtful organ in the abdomen may be safely diagnosed as kidney, if albuminuria follows after palpation. J. Schreiber (Zeit. f. klin. Med., Bd. lv).

Albuminuria may be discovered at one examination and not at the next, even the following day, *i.e.*, "fugal albuminuria," and may lead to errors in diagnosis. It is evidently the result of some interference with the circulation and may be encountered as a direct consequence of palpation of the abdomen. It occurs only when the epigastrium and mesogastrium are palpated, thus showing that the aorta above the renal arteries feels the effect of the palpating fingers. J. Schreiber (Med. Klinik, Apr. 4, 1909).

3. When the composition of the blood is altered, the urine often becomes albuminous. This can be proved experimentally by injecting egg-albumin, soluble casein, hemoglobin, etc., into the veins of animals; the quantity of albumin excreted after the injection will generally exceed the quantity injected. Similar results may be obtained by the injection of peptone and propeptone, whereas the albuminates are generally inoffensive. Ingestion of a very large quantity of egg-albumin is liable to provoke albuminuria.

Semmola has tried to prove that albuminuria is always caused by changes of the blood characterized by abnormal diffusibility of its proteids, and, in his opinion, the pathological changes in the kidneys are consecutive to the albuminuria. Though his theory is not generally accepted, Rosenbach has adopted it for the albuminuria which is not caused by nephritis, and regards it in such cases as a salutary and regulating process.

In most clinical cases different causes

are simultaneously active, and it is generally very difficult to determine which is the preponderating etiological factor. L. Williams ascribes the majority of cases of albuminuria either to altered blood states or to failure in the normal vasomotor mechanism.

> The majority of the cases are due to either altered blood states or to failure in the normal vasomotor mechanism. This failure may manifest itself in one or two directions. In the first, chiefly by some means so far undiscovered, the blood-pressure in the splanchnic area arises and is maintained at a sufficiently high level to induce a renal plethora and consequent albuminuria. Of such are the cases of hyperpiesis, as in the instance quoted. In the second place, owing to a local or general vasodilatation, the blood-pressure in the splanchnic area falls to the point at which a renal stasis is induced. Of such are the cases of cyclical, postural, and athletic albuminuria, of which also instances are cited, cases which, for the most part, occur in young adults in whom the vasomotor response is either undeveloped or for some reason is inadequate. Having regard to these facts, the writer ventures once more to insist not only that, of itself, albuminuria affords no evidence of renal disease, but that, of itself, it does not present even a reasonable suspicion of the existence of such disease any more than, of itself, dyspnea presents a reasonable suspicion of cardiac disease. L. Williams (Clin. Jour., Apr., 1908).

It is, nevertheless, true that traces of albumin, and even a rather considerable amount of it, may be found in the urine of persons otherwise healthy and presenting no symptoms of disease of the kidneys or of the organs of circulation.

Many clinicians, therefore, admit that albuminuria may be regarded, in some cases, as physiological; this is, however, contested by many.

> Case in which for over twenty years the patient had been passing large quantities of albumin in the urine, 3 grams per liter. Microscopic examination revealed no casts or corpuscles, and there was nothing to suggest renal trouble. The heart was normal in size, the sounds were normal, blood-pressure was in the limits of the normal, and there was little or no arterial thickening. The patient has maintained his usual high standard of health, and, although he had always been thin and spare, he is very tough. The most remarkable feature of the case, however, is that all the members of the patient's family exhibit the same peculiarity. They are all perfectly well, and, considering the age the parents have attained (87 and 78 respectively), such a case as this should have an important bearing on the question of rejection or "loading" of candidates for life insurance. Fergusson (Brit. Med. Jour., Mar. 19, 1910).

Virchow described a physiological albuminuria in infants, occurring in the first days of life, and explained it by the sudden changes of circulation taking place immediately after delivery.

Flensburg and Sjöquist have shown that albuminuria regularly occurs in the first days of life, and that the urine also contains an extraordinary quantity of uric acid crystals; probably the albuminuria is then due to the irritation of the kidneys caused by these crystals. Ebstein and Nicolaier have shown experimentally that when the kidneys are forced to excrete a surplus of uric acid which cannot be dissolved, but goes to the bottom in the form of crystals, the urine commonly contains albumin and sometimes even blood.

Gull found a certain form of physiological albuminuria in adolescents about the age of puberty, especially in weak and pale individuals. Other authors, among whom is Quain, have

noticed that this condition is quite frequently associated with masturbation.

Lommel found that 19 per cent. of young men (14 to 18 years old) suffered from albuminuria without having nephritis. The albuminuria had an intermittent character and was orthostatic in type.

> A large percentage of boys from 14 to 18 years of age suffer from albuminuria without having nephritis. Repeated examination of over 500 young employés of a large factory showed albumin in no less than 19 per cent. In most cases only traces could be detected, though in a few the amount exceeded 1 pro mille. The greater part of the albumin seemed to consist of lobulin, as in acute nephritis, indicating the presence of wide meshes in the filtering apparatus of the kidney. The cause of the albuminuria, which generally had an intermittent character and was orthostatic in type, was to be found in an impoverished condition of the blood, together with a mild degree of cardiac insufficiency and tendency to stasis, such as is liable to occur during puberty where the rapid growth of the body is out of proportion to the functional powers of the internal organs. In accord with this, dilatation of the heart, tension of the arteries, and accentuation of the second aortic sound were frequently noted. F. Lommel (Deut. Archiv f. klin. Med., Bd. lxxviii, Nu. 5 u. 6, 1903).

Dunhall and Patterson and Collier found albuminuria (0.2 to 15 per cent.) after severe exercise (such as rowing and running in races) also in healthy subjects.

> Several instances in healthy subjects in which albumin was found in varying amounts after severe exercise (0.02 to 0.15 per cent.). The writers also discovered incidentally that in different urines the sensitiveness of boiling and ferrocyanide of potassium with acetic acid, as tests for proteid, varied considerably. S. P. Dunhall and S. W. Patterson (Inter. Med. Jour., July 20, 1902).
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> As examiner of students at Oxford University, the writer has, during the past, been in the habit of advising all men whose urine showed the presence of albumin after exercise to give up all competitions involving great muscular strain, such as rowing and running in races. He found that if albumin was present during the student's first year at the university it continued throughout his career there. During 1906, however, he made systematic examinations of the various men in training for boat-racing, and found that, without exception, every man who rowed over the full course passed albumin in his urine, and at least one-half passed a considerable quantity. The same thing was true of the running men. So that just as evidence of hypertrophy of the left ventricle of the heart, and emphysema of the lungs may be expected in men indulging in violent athletics, so may the presence of a definite amount of albumin in the urine for a few hours after such exercises be looked for. The writer, therefore, no longer holds that such men should be advised to give up all hard athletic competitions, nor should insurance companies continue to refuse to consider the acceptance of the lives of such men. Collier (Brit. Med. Jour., Jan. 5, 1907).

PHYSIOLOGICAL CYCLICAL, ORTHOSTATIC, AND ORTHOTIC ALBUMINURIA.—The question of physiological albuminuria in adults has been much discussed during the past few years and has particularly engaged the interest of the medical men employed in insurance work.

It is characteristic of physiological albuminuria that the quantity of albumin is generally small and that the excretion is, in most cases, intermittent, or cyclical. Leube, Pavy, Fürbringer, Klemperer, and many other authors have studied this condition.

Pavy introduced the denomination "cyclical albuminuria" for the cases

in which the albuminuria ceases and returns at regular intervals.

Stirling ascribes cyclical albuminuria to a sudden shock from the blood-pressure upon assuming the upright position on arising, but Rudolph showed that albumin also appeared in the urine when the upright position was assumed very slowly.

Pavy likewise insists upon posture as the invariable cause of cyclical, or intermittent, albuminuria, the excretion ceasing when the subject is in the recumbent position and going on only when he is walking or standing. The cycles are commonly completed within the day, but in a case narrated by Klemperer there were two cycles, the maximum of albuminuria taking place in the forenoon and afternoon.

Hauser concludes that these cases can always be traced back to an uncured nephritis or to some acute infection (notably scarlatina), and puts no credence in a functional disorder. In other words, he always considers cyclical albuminuria as the expression of some pathological factor.

> The writer records a prolonged study of 14 cases of cyclical albuminuria, and concludes that these cases can invariably be traced to an uncured nephritis, or to some of the acute infectious diseases, especially scarlatina. The author does not believe that a functional disorder exists in these cases, but refers the appearance of albumin to excessive muscular use which affects the epithelium of the vessels of the glomeruli by an increase in toxins or in metabolic products. Hauser (Berl. klin. Woch., Dec. 14, 1903).
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> Case of a young man, 21 years of age, who had suffered for eight years from intermittent albuminuria that appeared as a sequela to an attack of nephritis caused by scarlet fever. Eichhorst (Med. Klinik, April 18, 1909).

Oswald attributes all forms of albuminuria of adolescence to irritation of the renal epithelium.

> There is no difference between the albuminuria of puberty and the so-called physiological albuminuria of adult life: between orthostatic albuminuria in a man and the puberal albuminuria of a boy. The writer considers that both are due to irritation of the renal epithelium. A. Oswald (Münch. med. Woch., 1904).

Moritz ascribes cyclical albuminuria to some insufficiency of the circulatory apparatus, having observed that the increased blood-pressure which normally occurs after moderate exercise is followed by abnormally low pressure in individuals that are subject to cyclical albuminuria.

> Cyclical albuminuria is due to some insufficiency of the circulatory apparatus, for the writer noticed that the increased blood-pressure which normally occurs after exercise of a moderate degree was followed by abnormally low pressure in those persons who were inclined to display a tendency toward cyclical albuminuria. He made some practical tests in two patients of this type by requiring them to lie down and then artificially inducing a disturbance of respiration by calling on them for straining efforts for ten or fifteen minutes, similar to those at stool. This was invariably followed by the appearance of albumin in the urine, although none had been present before. P. Moritz (Deut. med. Woch., Nu. 37, 1903).

The diagnosis of physiological albuminuria ought not to be made except in cases when persons presenting no other symptom of disease excrete, constantly or intermittently, a urine containing a scanty quantity of albumin, but no morphotic elements and especially no casts. The centrifugal apparatus, now in general use, will certainly contribute to restrain the number of these cases.

The urine should be obtained by catheterism in all doubtful cases.

The prognosis is generally considered good (Broadbent, Beck, Dukes, Tiessier, Posner). Nevertheless it is still justifiable for life-insurance examiners to be cautious in accepting persons suffering from albuminuria.

Orthostatic albuminuria is one of the functional albuminurias, and requires the erect posture for its appearance. It appears in young persons who are otherwise healthy, is not influenced by fatigue, habit to milk diet, and is not accompanied by any of the functional conditions associated with Bright's disease. The discovery is purely accidental, and depends upon methodical examination of the urine. Standing immobile will cause it to appear, and lying down to disappear. The albumin may persist while the patient is walking, but walking alone does not produce it. No functional disturbances in the other organs can explain this form of albuminuria. Orthostatic albuminuria occurs equally in both sexes, in neuropathic and slightly anemic adolescents, presenting a nervous or diathetic heredity, and is always associated with an appreciable disturbance of the vasomotor system. It seems to be due to fluctuating congestion of the kidney, a vasomotor disturbance of the renal circulation comparable to cyanosis of the extremities produced by the same cause. H. G. Beck (Amer. Jour. Med. Sci., Sept., 1903).

There is an affection which may be called postural albuminuria. Its characteristic feature is albuminuria on rising from bed in the morning, usually passing off in the course of the day. It is most common in boys and young men, especially those who are studying hard. It is not due to food, does not appear if the patient remains in bed to breakfast, and disappears quickly on lying down. It is obviously in relation with the erect posture after a night's rest in bed, and with imperfect cardiovascular adjustment to the changed hydrostatic conditions. The amount of albumin may be very small, but it is usually very considerable. Its recognition is important, as the treatment required is the exact reverse of the usual milk diet and protection from cold and fatigue.

The most common antecedent is a neurotic family history and cardiovascular instability. The pulse varies greatly in frequency and is greatly influenced by changes of position. The violent cardiac impulse is due to forcible action of the right ventricle, the apex beat being weak, and the second sound is reduplicated on lying down. The prognosis is favorable, all the treatment usually required being good, simple food; fresh air, and vigorous exercise. Tonics may be useful and constipation should be corrected. If these cases are treated for renal disease they usually go from bad to worse, and become confirmed nervous valetudinarians. Broadbent (Brit. Med. Jour., Jan. 2, 1904).

When the albuminuria of adolescents is recognized and treated, there is little likelihood of its proving the precursor of organic disease of the kidneys, even when its duration has been many years. The general treatment resolves itself into so reasonable a regulation of life as to insure the highest state of vitality during adolescence: *Work,* while it may be ample, must not be excessive; and work is always excessive during the years of growth, when sleep is insufficient. The hours of both must be determined according to age. *Exercise* should be recreation rather than physical drill, which, by the pleasurable sensations, increases the tone of the whole nervous and vascular system, and such exercise should be daily. *Food* should be sufficient for the provision of growth, as well as the removal of wear and tear, bearing in mind that the adolescent requires more food than the adult, and the girl more than the boy on account of her greater rapidity of growth. *The duties of the scavengers* of the body should be so disciplined as to be brought under the habitual control of the will. Natural action should not be replaced by the perpetual stimulus of aperients, for this

vicarious duty obviously confirms the intestines in sluggishness of work, and tends to convert a temporary inactivity into a permanent abandonment of function. Clement Dukes (Brit. Med. Jour., Oct. 7, 1905).

It is a mistake to diagnose a nephritis in every case where traces of albumin are excreted. With delicate tests albumin may be detected in almost every urine, but larger quantities often occur in the so-called essential albuminuria, and merely signify that the renal filter has become less dense without, however, altering the appearance or function to such an extent that a nephritis may be assumed. If the history of such cases be studied in detail, an infectious disease will often be discovered as cause, but even after years the amount, appearance, and specific gravity of the urine will remain normal and casts are uncommon or absent altogether. The treatment consists in proper diet and mode of living, since the kidneys undoubtedly form a *locus minoris resistentiæ,* and a nephritis may follow after the use of much alcohol, etc. C. Posner (Zeit. f. klin. Med., vol. liii, 1904).

It is no longer justifiable for life insurance and other such examiners to take the serious view hitherto accepted by most clinicians of physiological albuminuria. When it is found that the excretory function is being properly performed; that the substances normally gotten rid of through the kidneys are not being retained in the organism, and that the albumin in the urine may be diminished by lessening the hydrostatic pressure upon the renal capillaries by increasing the coagulability of the blood, there is every reason to conclude that the kidneys are free from organic disease, that life is not in the least endangered. Instances reported in which excellent results have been achieved by the administration of calcium chloride in doses of 20 grains three times a day. Calcium lactate in the same dosage is also useful. Both increase the coagulability of the blood. A. E. Wright and G. W. Ross (Lancet, Oct. 21, 1905).

Very small proportions of albumin should not be taken into account in relation to life insurance, and consequently the writer does not regard as of much moment the efforts to produce more and more delicate tests for albuminuria. The so-called physiological slight albuminuria after excessive exertion, sports, etc., may also be disregarded. The majority of cases of orthostatic albuminuria are also comparatively harmless; it is exceptional for nephritis to develop later in these cases. In examining it is important to note the absence of the higher blood-pressure characteristic of contracted kidney; also that the urine is free from albumin during reclining. Fürbringer (Deut. med. Woch., Nov. 25, 1909).

Teissier distinguishes three groups of orthostatic albuminuria: The *true orthostatic albuminuria,* where the albumin appears very soon after assuming the erect posture. It disappears in the recumbent posture. The *mixed orthostatic albuminuria,* which, more slow in its development (usually not before ten and twelve in the morning), is found in persons with an earlier acute infection and believed to be due to actual organic changes in the kidney. The *associated orthostatic albuminuria* is also slower in making its appearance after assuming the erect posture and is associated with abnormal conditions of other organs (dilated stomach, enteroptosis, movable kidney, etc.).

As nephritis can be excluded in the greatest majority of cases of orthotic albuminuria in children, a milk diet is contraindicated and a strengthening general diet indicated. In addition, there should be physical treatment to increase the general strength, with special attention to muscles of the lumbar region. Jehle (Münch. med. Woch., Jan. 7, 1908).

Examination of 150 girls between the ages of 9 and 14 to determine the influence of curvature of the spine on orthostatic albuminuria. It showed

that curvature of the spine is not the exclusive cause of orthostatic albuminuria, although it is an important factor in many cases by its interference with the circulation in the kidneys. Vas (Deut. med. Woch., Aug. 26, 1909).

Albuminuria in 4 girls between 12 and 16, nervous and anemic, but the albuminuria disappeared when the girls remained in bed. There was nothing but the albumin to indicate anything wrong in the kidney or circulation. The albuminuria could be induced at will by inducing lordosis. During the years of most active growth the vertebræ are not supported so firmly as later in life, and the physiologic curve of the spine becomes exaggerated by the laxness of the ligaments, etc. Turrettini (Revue de méd., Sept., 1909).

There are two indications to be followed: an avoidance of lumbar lordosis while standing or walking, and efforts to strengthen the muscles of the loins and abdomen in order to correct as quickly as possible the incorrect and harmful position. Fischel (Med. Klin., May 1, 1910).

Examination of 346 children between the ages of 5 and 13 for albuminuria showed that 14.5 per cent, 189 girls and 157 boys, gave signs of orthostatic albuminuria. There did not seem to be any more pronounced tendency to neuropathies among these children than among their mates, although enlarged tonsils or chronic pharyngitis were more frequent among them. There was no trace of pathological lordosis among a large number of the children, while true lordosis was quite frequent among children free from any tendency to albuminuria. F. Götzky (Jahrbuch f. Kinderheilk., April, 1910).

Even when no casts can be found, albuminuria ought never be regarded as absolutely inoffensive. Although a cyclical albuminuria continuing years may be compatible with perfect health, many authors (Johnson, Greenfield, Bull, etc.) are of the opinion that it signifies the first stage of the evolution of granular atrophy of the kidneys. On the other hand, casts may be found in normal urine and do not mean nephritis. Tuttle, for example, believes that nephritis may exist without albuminuria.

The mass of evidence which has come to us of late from the autopsy table shows conclusively that chronic nephritis exists and is an unrecognized cause of death in a proportion of cases far beyond ordinary belief, and the comparison of carefully kept records of cases before death with autopsy findings shows that little reliance can be placed on the mere urinary examination, either positive or negative, as a means of absolute diagnosis or prognosis of Bright's disease. The writer's own experience leads him to believe that (1) Bright's disease may exist without the ordinary urinary manifestations—viz., albumin or casts; (2) albumin and casts may be found in the normal urine and do not necessarily mean Bright's disease; (3) given a case of chronic Bright's disease with albuminuria, the fact of its presence, its constancy, or its amount has absolutely no prognostic significance. C. A. Tuttle (Jour. Amer. Med. Assoc., Mar. 31, 1900).

Series of experiments show that the albumin present in nephritic urine is derived from the blood and is different from the specific kidney albumins. L. Aschoff (Lancet, Sept. 6, 1902).

The albuminuria often found in parturient women (Aufrecht saw it in 56 per cent. of all cases) must be regarded as physiological.

Albuminuria occurring during labor is a reasonable accompaniment of parturition; the quantity is greater than can be considered normal, and is often the greatest seen in any except a permanent pathological condition. The condition requires no especial and separate treatment, and cannot be considered a permanent pathological lesion. The albuminuria of labor is differentiated from the other by the presence of labor and by the fact that it ceases

after parturition. The more abundant the albumin, the more gradual is its disappearance. The albuminuria of the puerperal period is the continuation of that of labor, and is never a separate condition. The albuminuria of labor is most pronounced toward the end of parturition, especially in cases of difficult or complicated labor. Circumstances which do not tend to make parturition especially difficult have no influence upon its albuminuria. The sediment of urine taken during labor shows organized material, including cylindroids, so often seen in cases of abundant albuminuria. These cylindroids are not abundant, and are to be distinguished from others by the fact that they contain superficial kidney epithelium in abundance, but not the elements which come from the deeper kidney structures. Jageroos (Archiv f. Gyn., Bd. xci, Hft. 1, 1910; Amer. Jour. Med. Sci., Nov., 1910).

PATHOLOGICAL ALBUMINURIA. — Pathological albuminuria is found in pathological changes of the blood—as anemia, leukemia, pseudoleukemia, scurvy, icterus, and diabetes —even when the kidneys do not present pathological changes.

It is also found in many disorders of the nervous system, as epilepsy, migraine, psychosis apoplexy, neurasthenia, and Basedow's disease, etc. Delirium tremens has also been mentioned as a nervous disease often complicated with albuminuria. H. H. Schroeder regards excessive eating, overindulgence in alcoholic drinks and possibly tobacco as the most frequent causes of albuminuria.

Transient albuminurias are not of serious import unless they occur too frequently. Persistent and even cyclic albuminurias should cause anxiety on the part of the attending physician, who should endeavor to ascertain the cause, and, if possible, remove it. A careful examination of these cases means a study of the twenty-four-hour specimen of urine. The daily quantity as well as specific gravity and amount of urea should be noted, and there should be an examination for albumin and casts. The blood-vessels should receive attention. Such observations might have to extend over months or even years. The most frequent causes of albuminuria are excessive eating, overindulgence in alcoholic drinks and possibly tobacco, and the gouty diathesis. H. H. Schroeder (Med. Rec., July 18, 1903).

Although the kidneys are theoretically believed to be healthy in the diseases mentioned above, there is no doubt that albuminuria, in many cases of this class, is caused by pathological changes of the kidneys.

In all febrile and especially in all infectious diseases albuminuria is a very frequent symptom. It has been noticed in enteric fever, diphtheria, variola, after vaccination, in erysipelas, influenza, rheumatic fever, pneumonia, etc. In these cases the albuminuria is caused by changes in the composition of the blood, increase of blood-pressure, rise of temperature, and finally by changes in the structure of the kidneys, especially of the tubular epithelial cells caused by the toxic substances excreted.

The presence of albuminuria in pregnancy, as stated above, is common (56 per cent.). Casts are only found in about 50 per cent. of these cases of simple albuminuria. The so-called kidney of pregnancy is to be regarded as a specific toxic nephritis which tends to recur in subsequent pregnancies. The prognosis of it, if properly treated, is good.

Albuminuria has been observed in diseases of the intestines, dilatation of the stomach, ileus, ruptures, etc., and in renal venous congestion caused commonly by disease of the heart or the great vessels.

It is present in all diseases of the kidneys. Acute, as well as chronic, albuminuria is generally found in the diffuse forms of nephritis, as well as in circumscribed renal diseases—such as infarcts, abscesses, or tumors. After retention of urine the portion of urine first passed is frequently albuminous.

> A large amount of albumin, without blood or pus, may generally be taken to indicate chronic tubal nephritis, and this can be confirmed by a high specific gravity, by microscopic examination, and by the appearance of the patient. A very small trace in an elderly or middle-aged man will probably indicate chronic interstitial nephritis; confirmatory evidence can be found in the aspect, the history, the pulse tension and tracing, the outward displacement of the cardiac impulse, the accentuation of the systolic apical sound, and the accentuation and reduplication of the second sound at the base of the heart. These indications may be further supported in some cases by the pale color and low specific gravity of the urine; less frequently information may be gathered from the presence of casts and from their predominant characteristics. The absence of casts is not, however, to be regarded as an indication that the case is not one of chronic interstitial nephritis. In a young man a mere trace of albumin may be the only evidence of a functional albuminuria, and the diagnosis must then rest upon negative evidence to a large extent, one of the most important factors being the relatively high specific gravity, unless this has been influenced by nervousness or by the recent consumption of a large quantity of liquid. With the same limitations the deep color of the urine will lend confirmatory evidence.
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> There are so many causes for great variations in the condition of the urine that stress cannot be laid upon the amount of albumin without paying due regard to most of the changes which have been touched upon by the writer. After all, albumin is merely an indication of an abnormal condition; it is not a disease. Therefore, as with every other symptom, by itself, it affords no reasonable ground for a diagnosis. Numerous other signs and symptoms must be carefully weighed, perhaps at short intervals, before it is justifiable to express more than a provisional diagnosis. Nestor Tirard (Lancet, Oct. 9, 1909).

Albumin is found in many diseases of the ureter, the bladder, the prostate and urethra. Ballenger speaks of prostatic albuminuria as a name for an albuminous secretion from an hyperemic or inflamed prostate. This prostatorrhea is constant by chronic prostatitis and often increases regularly every ten to thirty days. It should not be taken for a true albuminuria.

> In making insurance examinations as well as in the diagnosis of obscure forms of albuminuria, this possibility should be eliminated with the other sources of contamination before reaching a positive conclusion as to the significance of albumin. The periodic increase in the prostatic discharge, along with the striking similarity between the symptoms of intermittent, postural, orthostatic, and cyclical albuminuria and prostatorrhea, makes the possibility of mistakes in the diagnosis extremely likely when this fluid flows back into the bladder, and does not appear at the meatus. This regular increase every ten to thirty days and the analogy between the uterus and the prostate suggest a relation between the causes of this condition and menstruation. E. G. Ballenger (N. Y. Med. Jour., Feb. 24, 1906).
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> The writer means by alimentary albuminuria the passage of native food albumin, as such, unchanged from the alimentary tract into the urine. One should learn to recognize the existence of a distinct and well-characterized form of albuminuria of rather favorable prognosis that is not due to a nephritis

of toxic or infectious origin, to circulatory disturbances in the kidneys, to general cardiorenal disease (Bright's disease in the modern sense), but is due primarily to digestive disorders of a certain type. We are dealing here with an exclusively enterogenous albuminuria in the interpretation of which the renal idea proper should be largely relegated to the background and in which treatment should not, as in Bright's disease, be directed chiefly against disturbances about the general metabolism and the cardiovascular apparatus, but against a well-characterized perversion of the gastrointestinal and hepatic ductions. Croftan (Archives of Diagnosis, Oct., 1908).

Merk found that many affections of the skin, eczema, pruritus, urticaria, erythema, and furunculosis, are intimately associated with albuminuria. Gunzberger noted albuminuria during a severe attack of acute urticaria. Nicolas and Jambon and Boas hold that albuminuria is a frequent accompaniment of scabies, but it is not satisfactorily settled how it produces this phenomenon.

Albuminuria is a frequent accompaniment of scabies. The connection between scabies and albuminuria is not merely that of coincidence; it is not to be explained by the assumption that the subjects were already affected with renal disease and the itch was simply a casual acquisition, though persons who have been subjected to the ordinary causes of nephritis are more likely than others to be attacked with it in the course of scabies. The cutaneous irritation may of itself give rise to the kidney trouble through the mediation of the nervous system, but the manner in which scabies gives rise to albuminuria is by no means satisfactorily settled. J. Nicolas and A. Jambon (Annales de dermat. et de syphil., Feb., 1908).

Lancereaux observed frequently albuminuria in his cases of gouty, herpetic diabetes, but never noted it in his 40 cases of pancreatic diabetes. Glycosuria alone does not entail albuminuria. When it occurs it may be connected with arteriosclerosis, with subsequent lesions of the kidneys and heart, or be due to some intercurrent affection, tuberculosis in particular.

Certain remedies may also give rise to albuminuria.

The prognosis and treatment of albuminuria, therefore, depend entirely on the origin and causes of it, and the reader is referred to the various diseases in which it occurs as a symptom.

Investigations showing the existence in many cases of a direct relationship between the acid content of the urine and the amount of albumin and tube casts present. In the first case of albuminuria, the administration of phosphoric acid was found to cause an immediate increase in the albuminuria. In other words, with an increased acidity of the urine, there was a corresponding increase in the amount of albumin. On the administration, however, of alkalies in place of the acid, the albumin and tube casts diminished and finally disappeared. All the cases which were examined showed that, with increased acidity, there was increased albuminuria, and, corresponding with a diminution in acid, there is a diminution in the albuminuria. At the same time, in all cases of advanced grave kidney trouble, and especially in uremic patients, the relationship to acidity cannot always be demonstrated. The writer goes on to show that not only is the albuminuria lessened by alkali administration, but the functioning of the kidney is greatly improved and the very important excretion of chlorides is accelerated. The best mode of administration of the alkali is in the form of the ordinary sod. bicarb., which must sometimes be given in large doses. V. Hoesslin (Münch. med. Woch., Aug. 17, 1909).

TESTS.—By means of the tests commonly employed the presence of albumin in the urine is revealed, but no attempt is made to discern between the different proteids; the differential diagnosis between the serum-albumin, globulin, etc., will be given later on.

The sample of urine to be examined must be very limpid without deposits of any kind; if this be not the case, the urine should be filtered previous to the examination, because a slight cloud of coagulated albumin will only be discernible when the fluid is very clear before the reagent has been added. When the urine contains many bacteria, even repeated filtration will be insufficient to make it clear; this can then be done, however, by addition of a solution of sulphate of magnesia and of carbonate of soda. By shaking the mixture a precipitate of carbonate of magnesia is formed, and when this is removed by filtration the filtrate will be perfectly clear. In many cases a few drops of caustic soda will clear the urine, but urine treated in this manner will not give a precipitate of albumin by boiling, while the test of Heller is practicable also in this case.

Test by Boiling.—A few c.c. of urine are heated to the boiling point and some (5 to 10) drops of nitric acid added. When the urine is acid the albumin will ordinarily coagulate by boiling alone and precipitate as a whitish powder or in small flakes. The nitric acid is nevertheless in all cases to be added, as well in order to complete the precipitation of albumin as to avoid mistakes caused by the presence of a precipitate of phosphates or carbonates,—which will immediately dissolve when nitric acid is added. This test is very delicate and will reveal 0.01 to 0.005 per cent. of albumin. Instead of nitric acid, acetic acid can be employed, but, while the nitric acid is to be added after boiling and in a quantity of 5 to 10 drops, acetic acid is added before the boiling, and only a sufficient quantity (1 to 2 drops) should be employed as to make the urine but slightly acid. This is especially necessary when the urine is alkaline, because the alkaline albuminates with a surplus of acetic acid give a compound which is not coagulated by boiling.

Tretrop heats the urine nearly to a boiling point and adds a few drops of a 40 per cent. solution of formalin. The albumin coagulates like white of egg. After pouring off the fluid, the proportion of albumin can be determined by weighing the coagulum left.

Bychowski describes the following simple method to detect the presence of albumin, even if only a few drops of urine can be obtained: One or 2 drops of urine are put in a test-tube of hot water. After shaking, a whitish cloud is formed, if albumin is present. The test is very distinctive and is still more apparent when the test-tube is held against a black background. Of course, phosphates give the same reaction, but the cloud disappears on the addition of a drop of acetic acid.

Test for albumin in the urine in which the extra work of having a control or the filtering of the urine or the modification of its reaction has been eliminated.

Material needed for the test: Saturated salt solution, acetic acid, test-tube, pipette.

On heating urine three substances may be thrown down: albumin, nucleo-

proteid, and phosphates. About 5 to 10 c.c. of saturated salt solution, slightly acidulated with acetic acid, is heated to boiling in a test-tube. The urine to be tested is carefully allowed to run on top of the hot salt solution by means of the pipette. In order to make a good picture, the quantity of urine used ought to equal that of the salt solution.

By means of the heat in the saturated acidulated salt solution the above-mentioned substances are likely to be precipitated, but, owing to the contact, the saturated salt will not let the nucleoproteids appear, while the phosphates are also held in suspension by the acid; hence nothing can appear at the point of contact of the hot saturated salt with the urine except albumin.

Depending on the quantity of albumin present the reaction will be marked or only a film will appear overlying the clear, crystal-like salt solution. It is in urine with a trace of albumin in which this test shows extreme delicacy. The clear, crystal-like salt solution and the control-column of urine above with the surface of contact contrast quite decisively in distinguishing a delicate cloud.

Different pictures are produced in the great variety of urines by means of this technique:—

1. In clear urine which contains no albumin the delicate point of contact where the urine rides the hot salt solution is better brought out by setting the solution in motion by gently shaking the tube to and fro.

2. In clear urine sometimes a cloud appears some distance above the point of contact. This is due to the heat, which, traveling farther and faster than the acid of the salt solution, throws down a phosphate cloud.

3. Cloudy urine due to phosphates or urates is cleared at the point of contact because the acid and the heat dissolve these, respectively.

4. In cloudy urine due to bacteria no change is seen in the urine at the point of contact, and here, at times, only a close scrutiny of the urine above the crystal-like salt solution below in comparison with the zone of contact will give us the correct reading.

5. In urine containing albumin clouded by urates or phosphates, the albumin cloud at the contact differs in density from the remainder of the urine. Often the film of coagulated albumin is so delicate that the clearing of urates or phosphates is again seen above that of the contact zone.

6. In albuminous urine clouded by bacteria the coagulated albumin at the point of contact accentuates its presence by its difference in density.

It is in cloudy urine that the control of a clear, crystal-like liquid below the urine above emphasizes the beauty of the reaction in the zone of contact.

This test is a modification of the saturated salt, or brine, test, yet it adds to this old method the new qualities of diminished labor, simplicity, and accuracy. H. L. Ulrich (Jour. Minn. State Med. Assoc., Feb. 15, 1909).

Method of employing the acetic acid test for the detection of albumin which has long been used in France: 20 c.c. of urine, about three-fourths of a test-tube 1.5 cm. in diameter, are treated with 5 drops of 20 per cent. acetic acid, mixed, and one-half poured into a second test-tube. The contents of one tube are boiled, the other serving as a control. Albumin produces a cloud or precipitate in the boiled tube. Before testing, the urine must, of course, be perfectly clear; if necessary, it is shaken with Kieselguhr and filtered. If the acetic acid causes a cloud in the cold (nucleoalbumin), it is cleared by filtration before boiling. An alkaline urine should be acidulated slightly to prevent the precipitation of the phosphates, or, if a precipitate of phosphates appears when the urine has been treated with acetic acid and boiled, a few more drops of the dilute (20 per cent.) acid may be added to dissolve it. This will not redissolve even a slight albuminous cloud, provided the urine is not boiled again. Glaesgen (Münch. med. Woch., Bd. lviii, S. 1123, 1911).

Heller's Test.—Three to 4 c.c. of nitric acid are poured in a test-tube and a few c.c. of urine are cautiously filtered down along the sides of the tube without shaking the latter. The nitric acid rests on the bottom of the test-tube, and where the fluids are in contact a distinctly limited disk of grayish-white precipitate will appear. When only traces of albumin are present the precipitate will only take place after some minutes. The more or less distinct violet coloring which also appears at the point of contact of the two fluids is due to oxidation of indican or other chromogens. This test is very delicate and reliable; 0.003 per cent. of albumin is revealed by it.

Fallacies.—By the addition of nitric acid the urates or urea are also precipitated; these will not form a limited disk, but render the urine turbid. Resinous acids (copaiba, etc.) are precipitated by nitric acid, but are dissolved by the addition of concentrated alcohol. This error can be avoided by diluting the urine or by moderately warming the nitric acid before the test. Very often also a fine disk or ring will appear above the point of contact. This precipitation is due (Morner) to the presence of nucleoalbumins (mucin, chondrolin, sulphuric acid, etc.) and is more distinct after dilating the urine.

Test by Acetic Acid and Potassic Ferrocyanide.—The urine is rendered acid by acetic acid, and some drops of a solution of potassic ferrocyanide are added. This reagent, the serum-albumin, the globulin, and the albumoses are precipitated, while none of the normal constituents of the urine are (Huppert).

Heynsius's Test.—A still more delicate test than Heller's is that of Heynsius, by acetic acid and sulphate of soda. The urine is rendered acid by acetic acid, and an equal volume of a saturated solution of sulphate of soda (or of common salt) is added. The mixture is boiled, and all kinds of albumin will then be precipitated in white flakes.

The Magnesium-nitric Test (Roberts's).—One c.c. of nitric acid is mixed with 5 c.c. of a saturated solution of sulphate of magnesium, and a small quantity of this mixture is added to the urine. The albumin will be precipitated as a distinct ring.

Metaphosphoric Acid (Hindenlang's) also precipitates albumin in the same manner as nitric acid; but this test is not as delicate as that of Heller. The solution of metaphosphoric acid must be freshly prepared for use, as the solution easily changes to orthophosphoric acid upon standing, which does not precipitate albumin.

Picric Acid Test (Johnson's).—A few drops of a saturated solution of picric acid will cause a white precipitate when albumin is present; this test is only indicative of the presence of albumin, however, when the precipitate appears immediately. The urine must be acid. After some time the uric acid and the creatinine will also be precipitated (Jaffé).

Fallacies.—By addition of picric acid and peptones, the resinous acids,—such as those of copaiba,—and alkaloids—such as morphine—are precipitated.

Perchloride-of-mercury or Spiegler Test.—A solution of 8 grams of mercury, 4 grams of tartaric acid, 20 grams of glycerin in 200 grams of water produces a precipitate of albumin. The test is carried out in the same manner as Heller's test. It is very delicate (it reveals 0.0002 per cent. of albumin), but is not reliable when the urine is poor in chlorides (Jolles).

Millon's Test.—A solution of nitrate of mercury is added to the urine and the mixture heated to boiling. Nitrate of potash is then added; the albumin presents as a precipitate of red flakes. This test is disturbed by the sodium chloride of the urine and will be much better if tried upon the precipitate after boiling the urine.

Tanret's Test.—The reagent of Tanret is composed of perchloride of mercury, 135 grams; iodide of potash, 3.32 grams; glacial acetic acid, 20 c.c.; distilled water, sufficient to make 100 c.c.

Some drops of this mixture are added to the urine, when it will coagulate the albumin. It will also, however, precipitate the urates.

Tognetti described a "tannohydrochloric" test which reveals albumin, even in a proportion of 1 to 2,000,000. An equal amount of 1.5 per cent. alcoholic solution of tannin is added to the urine. After heating, an equal amount of 33 per cent. hydrochloric acid is added. A yellowish-white precipitate is gradually thrown down.

> The advantages of tannic acid as a reagent for albumin have long been known, but it could not be used in urine, as other ingredients of the urine also give a positive response. This difficulty has been removed by the adoption of the following technique, which, the writer says, renders the test reliable, instructive, and extremely sensitive. An equal amount of an alcoholic solution of tannin (1.5 Gm. of tannin in 100 c.c. of 90 per cent. alcohol) is added to the urine. The whole is then heated and an equal quantity of a 33 per cent. aqueous solution of hydrochloric acid is added—equal to the quantity of urine. In the presence of albumin the fluid becomes opaque and the albumin is gradually thrown down in a yellowish-white precipitate. In case of icterus, the bile pigments must first be removed by the Grocco technique, that is, by adding glacial acetic acid in the proportion of one-thirtieth or one-fiftieth of the amount of urine. With the exception of this precaution, which is necessary with other tests for albumin, the tannohydrochloric test, he declares, can be regarded as free from causes of error. The combination of tannic acid, hydrochloric acid, alcohol, and heat eliminates the usual drawbacks of tests for albumin. A. Tognetti (Gaz. degli Ospedali, vol. xxvii, No. 60, 1906).

Colquhoun recommends a solution of carbolic acid in absolute alcohol; this gives a white, milky precipitation of albumin. The test is said to show 0.002 per cent. albumin.

> A solution of carbolic acid in absolute alcohol is a very delicate test for albumin in the urine, comparing very favorably with nitric acid. The urine should first be diluted until the specific gravity is about 1.010; a few c.c. of carbolic acid are then poured on top of this, and a white ring is immediately formed, from which milky drops fall to the bottom of the tube, and adhering to this are the flakes of albumin. The test is sufficiently delicate to show 0.000012 gram in 1 c.c. of urine. W. Colquhoun (Lancet, May 6, 1900).

Many other reagents have been recommended, which cannot be mentioned in detail. The boiling test, Heller's test, the potassic ferrocyanide test, and the picric acid test are the most practicable and quite sufficient in general work.

Xanthoprotein Test.—Albuminous urine heated with a surplus of concentrated nitric acid will take a yellow color, and some of the albumin coagulates in yellow flakes, which are soluble in alkalies with an orange-red color.

> Very minute quantities of albumin may be detected in the urine by means of the deviation-of-complement test. For antigen the writer has used the serum of rabbits which had been immunized against human blood-serum.

When albuminous urines were diluted to such a point that they no longer gave a reaction with heat and acetic acid or with nitric acid, they still yielded positive results by the complement-deviation test, while in many instances albumin could be detected by this method in diluted urine when it could not be demonstrated by the ordinary chemical tests. The deviating power of the urine is not affected either by filtration through a Berkefeld filter or by dialysis. The antibody of the urine was, moreover, found to reside entirely in the serum albumin and serum globulin, and after the removal of the substances from the urine the remaining fluid no longer had the property of an antibody. C. H. Wilson (Jour. Path. and Bact., vol. xiii, p. 484, 1909).

Following are two new qualitative tests for albumin in urine, which are apparently specific as well as simple. The first test is with tincture of iodine and sodium bisulphate: A few c.c. (5 to 6) of the urine—which must, of course, be clear—are placed in a test-tube and acidified with a few drops of dilute acetic acid. About ⅕ volume of tincture of iodine (10 per cent.) is now added, and the whole is well shaken. A dirty, dark-brown precipitate results. A saturated solution (watery) of sodium bisulphate is next added drop by drop, shaking constantly, until the brownish fluid is decolorized. If the urine contains albumin, one sees a permanent whitish cloud or flocculent precipitate. If no albumin is present, the fluid remains clear after the addition of the sodium bisulphate, and shows only the original urinary color. With minimal quantities of albumin, the reaction becomes more evident on standing a few minutes. The second is with decolorized tincture of iodine: One decolorizes tincture of iodine with saturated watery solution of sodium bisulphate and filters. The filtrate is a clear, rather yellowish fluid, which keeps well. On standing for some time, small, yellow crystals may be precipitated, without injury to the reagent. The urine, as in the first test, is acidified with dilute acetic acid. About ⅓ volume of the reagent is added and the whole well shaken. If albumin is present, a cloud or a flocculent white precipitate forms. With traces of albumin the reaction may be delayed a few minutes. Normal urine never shows a cloud with these tests. Oguro (Zeit. f. exper. Path. u. Therap., Bd. vii, S. 349, 1909; Amer. Jour. Med. Sci., Jan., 1910).

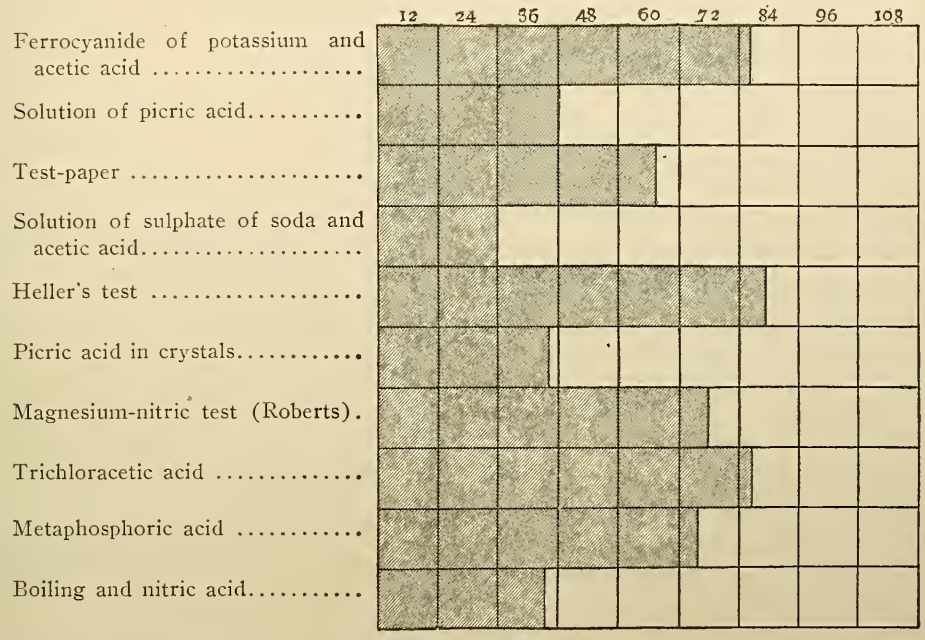
Aufrecht's method is to be preferred. It consists of centrifugating the urine, mixing with 4 c.c. of urine 3 c.c. of an aqueous solution of 1.5 per cent. picric acid and 3 per cent. citric acid. The results are reliable, while the method is simple, rapid, and practical, and can be applied to any organic fluids, and also for determination of propeptones in urine after filtering out the albumin, cooling and centrifugating anew. Koppang (Norsk Mag. f. Laegevidenskaben, Sept., 1910).

Transportable Reagents for Albumin.—Hoffmann and Aazette employ strips of test-paper previously placed in a solution of the double iodide of potassium and mercury until saturated, then removed and dried. Geissler's albumin-test paper is previously placed in a solution of citric acid. The urine which is to be tested should be clear and rendered acid by means of a few drops of acetic acid. If there be albumin present, upon immersion of a slip of paper in the urine a distinct precipitate will appear.

Pavy recommends test-pellets containing ferrocyanide of soda and picric acid; when albuminous urine is well shaken with a parcel of the pellet, albumin will be precipitated. Stütz and Fürbringer employ capsuloids of gelatin filled with perchloride of mercury, sodium chloride, and citric acid. The relative delicacy of the tests most frequently employed is graphically represented by Unger-Vetlesen, in the

diagram shown below. The longest columns indicate the most delicate tests.

Quantitative Tests. — The only method which gives fully reliable results is the gravimetric method. One hundred c.c. of urine are boiled upon a water-bath half an hour; if precipitation does not take place a few drops of a weak solution of acetic acid are added; the liquid is now brought on a weighed filter and the precipitate



repeatedly washed with hot water. The filtrate must once more be acidulated with acetic acid and boiled again, in order to ascertain whether the precipitation has been quantitative. When the water has been removed from the filter by strong alcohol, and the alcohol with pure ether, the filter is dried at a temperature of 110° to 120° C., and the percentage of albumin determined by weighing.

For clinical use several approximate methods have been invented.

Esbach employs an albuminimeter, *i.e.*, a graduated glass tube; this tube is filled to one mark (*U*) with the urine and then to the mark *R* with the test-solution consisting of picric acid, 10 grams; citric acid, 20 grams; water, 1 liter. The tube is then closed with a rubber stopper and the contents cautiously mixed (not shaken). The mixture is allowed to stand undisturbed for twenty-four hours and the quantity of precipitated albumin then read off. The reading indicates in grams the amount of albumin per liter. The urine must be acid, the specific weight should not be more than 1006 to 1008, and the temperature of the room approximately constant (15° C.). Resinous acids must be extracted with ether. The yellow crystals often found on the side of the glass are crystals of uric acid.

Christensen recommends another method: the albumin contained in 5

c.c. of urine is precipitated by 10 c.c. of a watery solution of tannic acid (1 per cent.). The albumin having been precipitated, 1 c.c. of an ordinary gum-arabic mucilage is added, the volume brought up to 50 c.c. with water, and the whole converted to an emulsion by agitation. Upon a piece of white paper, ruled with black lines 0.5 mm. wide and at equal intervals, is placed a cylindrical glass measuring 4 cm. in diameter. This is half-filled with water, and as much of the emulsion run in as possible without obscuring the black and white lines beneath the vessel. From the number of cubic centimeters required, reference to a table of calculations arranged by Christensen furnishes the proportion of albumin present in the emulsion. When the urine is alkaline it should be faintly acidified with acetic acid before the precipitation of albumin. This test can be made as well by daylight as by the light of a good lamp, and requires only ten or fifteen minutes; but is not applicable to urine containing a small amount of albumin, the variations amounting to two-thousandths.

The polariscope is sometimes employed to estimate the quantity of albumin, but this test is not reliable. It is true that albumin is levorotatory, but this is also the case with normal urine, and sometimes the color of the urine is too dark to allow the use of the polariscope.

Goodman and Stern have pointed out (1908) a quantitative method which gives results in a few minutes. It is based on the precipitation of albumin by phosphotungstic acid in the presence of a mineral acid. One gram of crystallized egg-albumin is dissolved in 100 c.c. of distilled water (solution A); 1 c.c. of this solution is diluted with 9 c.c. of distilled water (solution B). Drop in a test-tube 5 c.c. of the following solution:—

℞ *Phosphotungstic acid* ..... 1.5 Gm.
Hydrochl. acid (conc.) ..... 5 c.c.
Alcohol (95 per cent.) ..q. s. ad 100 c.c.

Now it takes 0.1 cm. (added with a pipette graduated in 0.1 c.c.) of solution B to cause a cloudy precipitate, *i.e.*, 0.0001 Gm. of albumin. The diluted urine is tested in the same manner.

Miscellaneous.—By the tests above mentioned, as well qualitative as quantitative, the different coagulable proteids contained in the urine are precipitated; it is rarely of any use to differentiate them one from another.

Pure globulinuria without the simultaneous presence of serum-albumin does not occur. In order to precipitate the globulin alone the urine is rendered alkaline with solution of ammonia, after some time filtered, and the filtrate mixed with an equal volume of a saturated solution of sulphate of ammonia. If globulin be present a flaky precipitate will appear.

[The same result can be obtained by using a solution of sulphate of magnesia, which does not precipitate the other proteids of urine, or by diluting the urine until it reaches a specific gravity of 1002 and leading a slow current of carbonic acid through it for two or four hours. After twenty-four to twenty-eight hours the globulin will be precipitated. LEVISON.]

The albumoses often found in the urine seem to be a mixture of deuteroalbumoses and protalbumoses.

F. LEVISON
AND
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Copenhagen.

ALCOHOL.—Alcohol is one of a group of hydrocarbon compounds which have as their base a radical designated as ethyl, chemically represented by the formula C_2H_5. Alcohol is a hydrate or hydroxide of ethyl—C_2H_5OH. To distinguish it from other more toxic members of the series of alcohols, particularly fusel oil (chiefly amyl alcohol) and wood spirit (methyl alcohol), the spirit used in medicine is called ethyl alcohol. It is obtained by distillation and subsequent purification from a fermented mash of potatoes or grain, from fermented sugar, or from wine, and is known in the British Pharmacopeia as rectified spirit.

Absolute alcohol, *i.e.*, alcohol at least 99 per cent. pure, occurs as a volatile, inflammable, colorless liquid, with a characteristic pungent odor and burning taste. Its boiling point is 172° F. (77.7° C.). It has a marked affinity for water, which it abstracts from whatever substances it may be in contact with, including the air and the human tissues. It is miscible in all proportions with water, glycerin, ether and chloroform. When absolute alcohol is mixed with water the resulting volume of fluid is slightly less than the sum of the two components before their admixture.

Alcohol is a solvent for resins, volatile oils, fats, and alkaloids, and is very extensively employed as such in preparations containing remedies of these classes, most of which are insoluble in water. It forms the menstruum in the official tinctures, spirits, elixirs, and all but two of the fluid-extracts.

PREPARATIONS AND DOSE.

Alcohol contains 94.9 per cent. by volume (92.3 per cent. by weight of pure ethyl alcohol to 5.1 per cent. of water). Specific gravity, 0.816. Rarely used internally in doses of 1 to 4 drams, diluted with water.

Alcohol Absolutum (Absolute Alcohol) contains not more than 1 per cent. by weight of water. Specific gravity, 0.797.

Alcohol Dilutum (Diluted Alcohol).—A mixture of alcohol and distilled water, containing 48.9 per cent. by volume (about 41.5 per cent. by weight) of pure ethyl alcohol to 51.1 per cent. of water. Specific gravity about 0.937.

Spiritus Frumenti (Whisky).—44 to 55 per cent. by volume of absolute alcohol.

Spiritus Vini Gallici (Brandy).—46 to 55 per cent. by volume of absolute alcohol.

Vinum Album (White Wine).—8.5 to 15 per cent. by volume of absolute alcohol.

Vinum Rubrum (Red Wine).—8.5 to 15 per cent. by volume of absolute alcohol.

Whisky is produced by the distillation of fermented grain (rye, corn, or barley), and brandy by the distillation of fermented grapes. Inasmuch as the toxic amylic alcohol is likely to be present in freshly distilled spirits, the Pharmacopeia specifies that these products shall have been kept in storage for a certain period before use (whisky, two years; brandy, four years), the amylic alcohol becoming oxidized into harmless ethers. White wine results from the fermentation of the juice of fresh grapes, from which the skins, seeds and stems have been removed, while red wine is produced from purple-colored grapes with the skins included. The latter contains more tannin, but less tartaric acid than white wine.

Dose.—The ordinary dosage of whisky or brandy in adults unaccustomed to their use may be said to range

from 1 dram (4 c.c.) to 2 ounces (60 c.c). In regulating the dose the capacity of the individual to oxidize the alcohol is to be taken into account, the object being, if alcohol is to be given repeatedly, to limit the amount to that which can be destroyed in or eliminated from the organism in the interval between successive doses. According to Bartholow, the quantity which a healthy adult is able to oxidize in twenty-four hours is from 1 to 1½ ounces of absolute alcohol. Where this is exceeded, an accumulation of the drug in the system is likely to occur, and the following symptoms may be expected to appear. Flushing of the face, dryness of the skin and mucous mebranes, bounding pulse, and the odor of alcohol on the breath. Such signs indicate, in any given case, that the useful amount of alcohol, whether employed for general or merely for digestive stimulation, is being exceeded. In persons habitually taking alcoholic beverages the ability to oxidize alcohol is augmented, finding its expression in increased tolerance; hence in these individuals, if alcohol is given for the purpose of obtaining therapeutic effects, the dose will have to be increased, and even, in many cases, doubled or tripled. In febrile states large amounts have often been administered without causing signs of intoxication, the oxidizing power evidently being heightened during the febrile process; notwithstanding this fact, it is now generally considered that small doses of alcohol—if, indeed, it be used at all in these cases other than during periods of dangerous circulatory depression—will give as good results as large amounts.

In children, as well as in the aged, alcohol is well borne. To the former it can be administered in doses proportionally larger than are suitable for adults, while in the latter the dose need not be reduced from that given to the middle-aged.

MODES OF ADMINISTRATION.—Alcohol, as used in therapeutics, is usually exhibited in dilute form in one of the various spirituous beverages, the majority of which are non-official. They may conveniently be grouped according to the percentage of alcohol contained.

The so-called "spirits" include whisky, brandy, gin, rum, and arrack, and all contain about 50 per cent. of alcohol. A liquor having this percentage is said to be "proof spirit," implying that it contains just sufficient alcohol to be inflammable. Gin ("spiritus Genevæ") is made by adding oil of juniper berries to rectified alcohol or whisky. The official *spiritus juniperi compositus,* with 4 per cent. of juniper oil as well as other flavoring substances, is a preparation similar to gin, but is stronger in alcohol, containing 70 per cent.; the average dose is 2 drams. Rum ("spiritus Jamaicensis") is obtained by distilling fermented molasses or sugar. Like gin, it is not official. Arrack results from the distillation of fermented rice. Spirits contain a large number of other volatile bodies besides the main component, ethyl alcohol. These include higher members of the same group of alcohols as ethyl alcohol, as well as alcohols of other series and a group of bodies the composition of which remains obscure, known as the œnanthic ethers, and which, though present in small amounts, give to the various liquors their characteristic flavors. Spirits differ radically from wines in that they are free of non-volatile compounds, which are left behind in the process of distillation.

The heavy wines contain about 20 per cent. of alcohol, being made from grapes

having a large proportion of sugar. They include port, sherry, Madeira, Marsala, Malaga, and others. Port (formerly official as "vinum portense") is a sweet, red wine, containing 15 to 22 per cent. of alcohol; its sweetness is due to arrest of the process of fermentation while still incomplete. Sherry ("vinum Xerici") is a white wine, containing 15 to 18 per cent. of alcohol. Port and sherry of American production are usually lighter, the percentages ranging from 10 to 18. Madeira is a dark-colored white wine with 18 to 22 per cent. of alcohol. Marsala is a wine similar to Madeira, but of Sicilian production. Malaga is a sweet wine, having 17 per cent. of alcohol. The heavy wines are, in general, too sweet for the use of sick persons; when obtained "dry" (free, or nearly free, from sugar), however, they are frequently of benefit to convalescents and to the debilitated.

The light wines contain from 5 to 15 per cent. of alcohol. Ordinary claret ranges from 6 to 12 per cent. This group also includes Burgundy, the Rhine wines, Moselle, Tokay, champagne, and hock, in all of which the percentage of alcohol is usually between 9 and 14. Champagne, though it contains only about 10 per cent. of alcohol, has a pronounced stimulating effect on the gastric mucous membrane because of the large amount of carbon dioxide it liberates. Wines are more slowly absorbed than alcohol, and the physiological effects of the alcohol they contain are correspondingly less marked. In addition, wines possess distinct nutritive value, by virtue of the numerous substances, both organic and mineral, which they embody. These include, according to an analysis of red wine by Gautier, albuminoid, fatty, and carbohydrate constituents, glycerin, potassium tartrate, succinic acid, acetic, citric, malic and carbonic acids, and salts such as the chlorides, bromides, iodides, fluorides, and phosphates of potassium, sodium, calcium and magnesium oxide of iron, etc. Wine also contains a number of volatile bodies, such as are present in brandy in larger amount. Light wines are useful wherever prostration is or has been a marked feature of the case, *e.g.*, in **typhus, intermittent fever, scurvy,** and **cholera** among the more acute diseases; also in many chronic affections, excluding, however, cases of **Bright's disease, chronic digestive disorders, neurasthenia, anemia,** and **diabetes.** Wines are peculiarly liable to undergo acetic fermentation in the stomach (Hayem), and hence are not well borne in certain gastric disturbances. It has been found *in vitro* that wines uniformly interfere with peptic digestion. Red wines very usually disagree where there is gastric hyperacidity. In these cases white wines are generally serviceable. White wines have a diuretic effect beyond that possessed by the red wines. When very acid, however, they are in themselves capable of causing gastric disorders, and should be avoided wherever diarrhea exists. Many of the Rhine wines are not suited to those having a tendency to the formation of oxalic deposits, owing to the oxalic acid which they contain.

Malt liquors (beer, ale, brown stout, porter) contain less alcohol but have greater nutritive value than any other of the alcoholic beverages. They are produced by causing an extract of malt (sprouted barley grains) and hops to undergo fermentation by the yeast-plant. The malt is previously allowed to germinate, in order that the starch it contains shall be transformed into the

more easily fermentable sugar. The diastase which effects this conversion is formed by the grain itself during germination. The yeast then ferments the sugar with the production of alcohol. The final product contains about 3 to 7 per cent. of alcohol and a large percentage of solid constituents available for nutrition, including mainly dextrin, sugar; albuminoid, fatty and gummy substances; succinic, lactic and acetic acids; aromatic and bitter principles derived from the hops, carbon dioxide to the extent of 6 to 8 times the volume of the liquor, and a number of salts resembling those found in the ashes of meat extract, principally phosphates and salts of potassium and calcium (Manquat). Beers also contain diastase, which aids in the digestion of carbohydrate foods and tends to produce obesity. Ale differs from beer in that its fermentation is carried on at a high temperature instead of a low one; it usually has a higher percentage of alcohol, ranging from 4 to 8 or 9 per cent., while beer has 2 to 6 per cent. (4 per cent. on the average). Porter and brown stout are fermented at a still higher temperature; some of the sugar is converted to caramel, giving these beverages their darker color. They contain 4 to 6 per cent. of alcohol.

When the digestive powers are but little impaired, beer is valuable as a tonic and nutritive. The hops and the carbon dioxide probably both stimulate functionally the gastric mucosa. Where the digestion is weak, the large dextrin and sugar content of beer may undergo fermentation in the stomach. The absorption of beer is, in any case, slower than that of other liquors. Beer diluted with water is said to be better borne than wines where there is hyperchlorhydria. The low percentage of alcohol contained in beer renders it useful where the patient appears specially sensitive to the action of alcohol on the cerebrum. A syrupy extract of malt is official in the United States Pharmacopeia as *extractum malti;* it contains large proportions of dextrin, sugar, phosphates and nitrogenous bodies, and but 2 per cent. of alcohol.

Less important medically are the wines of other fruits than the grape, and the liqueurs. Among the former may be mentioned cider, which results from the fermentation of apples and contains 2 to 5 per cent. of alcohol, and perry, a similar product made from pears. Cider is useful where diuretic and slightly laxative effects are desired. Liqueurs comprise a large class of alcoholic products differing widely in composition. They are generally made by the addition of essential oils; they frequently contain a large amount of sugar, and are of but little value in therapeutics.

In acute diseases alcohol is usually given internally in the form of whisky or brandy.

CONTRAINDICATIONS.—Alcohol is contraindicated in nephritis and inflammatory conditions of the urinary passages, in conditions associated with marked gastric or intestinal irritation, and in persons likely to acquire the alcoholic habit,—especially young adult or middle-aged neurotics, and persons who have been subjected to traumatism of nervous structures. In prolonged cardiac depression alcohol is likely to do more harm than good. Sweet wines and beer are contraindicated in diabetes mellitus and in eczema. In the diarrheas of children alcohol should not be administered unless the stomach and bowels have already been freed from putrefying material.

Protest against alcohol in any form in ptosis of the stomach or intestines, as this is not a local affection, but is associated with nervous and other disturbances. The physical and nervous disturbances which forbid the use of alcohol in cases of enteroptosis in many cases do not develop until the age of 25 to 28. Concussion of the brain contraindicates alcohol; many physicians refuse to treat traumatic nervous affections unless the patients go to a hospital where abstention from alcohol will be enforced. Traumatic nervous affections tend to induce hysteria, and the necessity for abstention from alcohol in hysteria and neurasthenia and conditions of dread and compulsion can never be too often emphasized. The patient is chained to his crutch and soon is unable to do without it if alcohol is given to relieve him. A psychic trauma of any kind should contraindicate alcohol, as it is particularly liable to act abnormally in abnormal psychic conditions. This includes the period before and after an operation. Abstention from alcohol is an important factor in the warding off of the after-affection of gonorrhea and syphilis. The worst forms of tabes occur among those who take alcohol, and the lesser consumption of alcohol is one reason why women have the milder form. Among the injurious influences of syphilis must be counted, besides the virus, the emotional distress, the knowledge of the disease, the psychic depression and the necessity for secrecy, all of which render alcohol particularly injurious for syphilitics. Röder (Med. Klinik, Nov. 8, 1908).

Syphilis is always badly affected by alcohol, and the latter is responsible for many of the evil results often seen in this disease, both in the skin and in the nervous system. The syphilitic should be an abstainer from alcohol from the moment of his infection. Acne constantly shows the effect of drinks containing alcohol, the condition varying more or less according to the character of the beverage. The acne rosacea of tipplers is well known, and this is often followed by a permanent dilatation of the capillaries of the face and hypertrophy of the nose, resulting even in rhinophyma. In beer and ale drinkers the eruption is of a more pustular character, often with large lesions. Eczema is often profoundly affected by alcoholic beverages, which might render the disease incurable when they are persisted in, even in moderation. Psoriasis is greatly aggravated by the indulgence in alcoholics and is caused to itch by such indulgences; the use of alcohol can also induce a fresh attack after a long period of freedom from the eruption. In cases of even moderate drinkers the disease yields much more quickly under total abstinence. L. Duncan Bulkley (Med. Rec., Jan. 29, 1910).

PHYSIOLOGICAL ACTION.—The effects of alcohol, when it is taken internally, vary according to the size of the dose. The action here to be described is that of therapeutic or somewhat larger doses.

Digestive Tract.—In the mouth and pharynx, alcohol has a slightly astringent action upon the mucous membranes. For a brief period it also causes an increased flow of saliva, and when in no greater concentration than 5 per cent., has been found by Störck to favor the digestion of starchy foods by ptyalin. The action of ptyalin is, on the contrary, unfavorably influenced by alcohol in 10 per cent. strength and, more particularly, by the acids contained in malt beverages and wines.

On reaching the stomach, alcohol produces a sense of warmth, which is promptly followed, as absorption takes place, by a general feeling of well-being and restfulness. When present in the stomach in small amount only, alcohol has no marked effect on peptic digestion, and often distinctly augments the

secretion of gastric juice, itself becoming thereby progressively more dilute. It acts both by stimulating directly the gastric circulation and the secreting cells to greater activity, and probably also by a special secretory influence of the alcohol after its absorption. Since Spiro, Frouin and Moulinier observed that alcohol administered per rectum caused in the stomach a marked flow of abnormally acid gastric juice. Chittenden and Mendel showed, moreover, that the relative amounts of pepsin and hydrochloric acid in the gastric juice were both increased. Thus alcohol in small quantities tends to hasten gastric digestion. Fatty substances being dissolved by it, their absorption is facilitated. The appetite, when poor, is improved.

When 5 to 10 per cent. of alcohol is present, peptic digestion takes place less rapidly than normal, the degree of interference varying with the kind of food to be acted upon. According to Klemperer and Battelli, however, gastric motility is hastened by moderate amounts of alcohol, while Bandl, Scanzoni and others have shown that liquids containing alcohol are much more rapidly absorbed from the stomach than liquids free of it. It thus happens in many cases that the interference of the alcohol with peptic digestion is more than counterbalanced by the hastened absorption as well as by the increased amount of gastric juice. Gluzinsky's experiments indicate that alcohol slows gastric digestion only during the period before its absorption; it then causes increased rapidity of digestion because of the special stimulating effect on secreting structures already mentioned. According to this author 60 Gm. (about 2 fluidounces) of cognac, taken during or before a meal, slows the digestion of carbohydrates and hastens that of meats, but when taken after the meal hinders both. It has been noticed that spirits are much less potent in hampering peptic activity than are wines and especially malt liquors.

> Series of experiments to determine the influence of alcohol upon the secretion of the gastric juice: upon a case of gastroptosis, one of hysteria, one of atony of the stomach, after gastro-enterostomy, and one of gastro-enteritis. The alcohol was administered per rectum, and the patient took no nourishment by the mouth. It was found that the enema caused an active secretion of gastric juice provided the amount of alcohol was not less than 7 to 10 c.c. The acidity reached its maximum about an hour after the injections, and then gradually decreased. In two cases of achylia due to carcinoma of the stomach no effect was observed. R. Spiro (Münch. med. Woch., No. 47, 1901).

Alcohol passes quickly from the stomach into the intestines. Here also it is absorbed, and exerts, when in small amount, an effect similar to that produced on the stomach, viz., stimulates the mucous and other glands to increased activity. Relaxation of the bowels and meteorism are frequently influenced by it. *In vitro* alcohol in 3 per cent. strength, however, slows the digestion of proteids by the pancreatic juice (Chittenden and Mendel).

Nervous System.—When the action of alcohol has been exerted long enough, it acts as a depressant to the nervous system. The effects seen at first suggest primary cerebral stimulation, but it is a question whether these phenomena are not really the result of impaired inhibition, in which case alcohol might be said to act as a depressant from the beginning. Small amounts of alcohol do, indeed, produce effects sug-

gesting loss of inhibitory control over cerebral activities, though it must be admitted that the actual physiological existence of such a controlling function has not yet been definitely proved. In the primary stage of apparent excitation, the subject exhibits loss of control, as manifested by loose speech, laughter upon slight provocation, outbursts of the passions and exaggerated movements. The subject becomes selfish, irresponsible, and lacks will-power. Bunge, Schmiedeberg and others believe that these phenomena occur because the normal inhibitory influence on the cortical centers has been reduced.

As an argument against the theory of primary stimulation it is pointed out that a primary stage of excitement is usually not seen when the subject remains in quiet and dark surroundings after taking alcohol, while certain individuals show no evidences of stimulation under any circumstances, but soon pass into a state of cerebral depression. Other observers believe that the physical excitement and the unusual flow of ideas and powers of speech often observed under the influence of alcohol indicate a primary stimulating effect on the same centers. The ability to perform muscular work has usually been found in experiments to be increased for a brief period by alcohol in small amounts, especially where fatigue exists, but this is very promptly followed by a distinct decrease; further, it is not proven that the preliminary increase is due to excitation of the motor areas, since the nerves or muscles themselves may instead have been affected. Kraepelin concluded from his experiments that motor activities were heightened by alcohol in small amounts and depressed by larger quantities, but that the mental activities were lowered for a period of twelve to twenty-four hours by it even in small doses. Alcohol acts also on certain sensory centers, reducing pain.

> After taking small amounts of alcohol there is an apparent temporary increase of brain-activity, which is but an evidence of the paralyzing and deleterious effect of alcohol. It destroys the special function of the cerebellum, and produces tremor and weakness of the lower limbs. In chronic alcoholism the dendrites of the pyramidal nerve-cells show swellings and shrinkages, and there is widespread pigmentation in the nerve-cells. Even small doses of alcohol at meals have a deleterious influence, and total abstinence must be the course of those who wish to follow the plain teaching of truth. Victor Horsley (Lancet, May 5, 1900).
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> With our present knowledge it may be said that alcohol furnishes energy for muscular work in the same manner as fats and carbohydrates. There is no reason for believing that the muscle-cells cannot burn alcohol as they do other foodstuffs. However, from the standpoint of ability to do strenuous muscular work, there is evidence that a man cannot do as much work in the long run with alcohol as with carbohydrates. Mountain-climbers and athletes cannot do their best work when alcohol forms a part of their diet. This effect is explained by the drug action of alcohol upon the nervous system. Scarbrough (Yale Med. Jour., Feb., 1910).
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> Tests carried out on himself by the author through a number of months to determine the influence of a small amount of liquor on the power of concentrating the attention on and remembering twenty-five lines of a translation of the Odyssey, the blank verse being especially adapted for such tests. The alcohol had an unmistakable influence in reducing the powers of perception, and this effect was twice as marked on a fasting stomach. Vogt (Norsk Mag. f. Laegevidenskaben, June, 1910).

After the initial stage of apparent stimulation, the actual depressant action of alcohol on the nervous system is no longer in doubt. Soldiers have been found to march better and remain stronger without alcohol than when supplied with it in moderate amounts. Large single doses produce signs of distinct brain depression, passing from muscular inco-ordination, with imperfect speech, impaired sensibility, and somnolence, to a state of unconsciousness similar to that of ether and chloroform anesthesia. The spinal cord is depressed by alcohol even before the unmistakable signs of cerebral depression occur, as shown by the early muscular inco-ordination (apart from disturbances of equilibrium) and diminished reflex irritability. The functions of the bulbar centers, however, are not markedly affected until late. On the peripheral nerves alcohol in large doses was found by Dogiel to exert a pronounced depressing effect in dogs. Motor nerves are believed to withstand this effect longer than sensory nerves. In the frog the response of the motor nerves to stimuli is at first increased when the vapor of alcohol is brought in contact with it, but the usual depressant action soon follows.

Circulation.—Although the pulse-rate is commonly increased after the use of alcohol in considerable amount, Jacquet believes that where the subject can be kept free from external exciting influences, no such change in the heart-action is produced. The results of experiments intended to develop the action of alcohol on the heart have been contradictory. It is thought by many that the mammalian heart is slightly stimulated by alcohol unless given in large amounts, when it is depressed (Dixon and Bachmann, Wood and Hoyt, Loeb, Bachen). Alcohol in 2 per cent. strength passed through the coronaries of a cat's heart does not cause arrest of cardiac activity (Loeb). Other experimenters conclude that alcohol causes no increase in the work performed by the heart. According to Cushny the preliminary action of alcohol is to weaken the heartbeats. As for the blood-pressure, moderate doses have usually not been found to alter it. The advocates of primary cardiac stimulation by alcohol account for this by the dilatation of the peripheral blood-channels, which is often manifest in the flushed face, injected conjunctivæ, and heated skin surfaces observed after the use of alcohol. The speed with which the blood courses through the vessels is thereby increased (Hemmeter, Wood and Hoyt). Whether the vascular dilatation is due to an action on the vasomotor centers or on the vessels themselves has not as yet been determined. The results include disturbances in the cerebral circulation; the brain may be the seat either of marked hyperemia or of anemia (Claude Bernard). Certain experimenters have at times observed increased blood-pressure due to alcohol; thus Kochmann noted in man a rise in the pressure upon the exhibition of 5 to 10 c.c. (1¼ to 2½ drams) of absolute alcohol. Such an elevation of pressure might be due either to a direct stimulating effect on the vasomotor centers, or, as many believe, to a reflex effect on these centers due to irritation of the gastrointestinal mucous membranes.

> The contact of strong alcohol with the mucous membranes of the mouth, esophagus, and stomach acts reflexly through the medulla to cause vaso-constriction, which raises the blood-pressure, and hence stimulates the

heart. After alcohol is absorbed (it circulates as alcohol) it causes vasodilation and a fall in blood-pressure. It is certain that overdoses of alcohol after absorption are depressant to the heart-muscle, to the muscle-fibers of the blood-vessel walls, and to the vasomotor center in the medulla. On these considerations the author bases his advice on the use of alcohol in derangements and affections of the heart. With regard to the utility of alcohol in combating poisons circulating in the blood, clinical experience is not conclusive. Laboratory experiments should be undertaken in order to settle this point. O. T. Osborne (Jour. Amer. Med. Assoc., Dec. 5, 1903).

Experiments performed in rabbits, supporting the belief that the acceleration of the heart after the use of alcohol is a gastric reflex from irritation, and that when the reflexes have been abolished as a result of the anesthesia, the quickening of the heart and the subsequent rise in pressure from alcohol do not occur. A similar effect upon the circulatory system can be produced by other gastric irritants, such as ammonia, ether, and capsicum. McNider (Charlotte Med. Jour., Aug., 1909).

Report concerning a series of manometric blood-pressure tracings showing the effect of alcohol on dogs not under the influence of any anesthetic. The primary action of alcohol was found to vary according to the mode of administration: By mouth it caused a marked rise in blood-pressure, with increased amplitude and a constant, or slightly slowed rhythm of heartbeat. This rise gradually passed off in five or ten minutes. In some instances, at the time of pouring the alcohol into the dog's throat, and just preceding the rise mentioned, there was a sudden drop and almost immediate recovery of blood-pressure. When given intravenously alcohol caused a sharp drop in blood-pressure, during which the heart was greatly slowed or almost stopped; but very soon, unless the dose was too large, there followed a rapid recovery. Upon administration of alcohol by gastric fistula there was no specific primary action. By whatever method administered, alcohol, when circulating in the blood-stream, causes a gradual, progressive lowering of blood-pressure with decrease in amplitude, but increase in rate of heartbeat. Clyde Brooks (Jour. Amer. Med. Assoc., July 30, 1910).

Excessive amounts of alcohol cause a pronounced fall in the blood-pressure, since they depress both the heart and the vasomotor center. They have also been observed in animals to slow the heart action, and even produce cardiac arrest, in much the same manner as does chloroform. According to Pouchet, the secondary fall of blood-pressure is due largely to stimulation of the inhibitory pneumogastric centers; the pressure may, indeed, at a certain stage of the poisoning be brought almost back to normal by section of the vagi.

Retardation of the pulse is brought about by an irritation of the vagus centers, and of the peripheral ends of the vagi, in part due to a direct cardiac action. The fall in blood-pressure is due to a direct injurious influence upon the heart-muscle. Ladislas Haskovec (Wiener med. Blätter, Oct. 11, 1900).

Experiments to determine whether alcohol, coming in direct contact with the heart muscle, would act as a stimulant to the action of that muscle or not. The author feels justified in concluding that alcohol is not a stimulant to heart muscle, but rather a depressant and a poison. A. W. Downs (Monthly Cyclo. and Med. Bull., March, 1911).

Blood.—Large amounts of alcohol must be present to cause perceptible changes in the blood in a short space of time. Foguet claimed to have ascertained that intoxicating doses, taken daily, were without effect. Pouchet

states, however, that under small, repeated doses, the blood gradually undergoes fatty changes, owing to the fact that the emulsified fats entering the blood with the chyle are not consumed as normally. At the same time the alkalinity of the blood is lowered, the coagulability rises, and a process of dehydration goes on, as shown by diuresis and increased secretions generally, whereby the blood becomes relatively more concentrated, the erythrocyte count and hemoglobin percentage rising. Schmiedeberg found that blood containing alcohol loses in part its oxygenating power,—a fact of considerable practical significance. *In vitro,* alcohol added to blood darkens its color, coagulates it, and causes hemoglobin to leave the erythrocytes. Such effects can only be obtained in the animal organism by the intravenous injection of alcohol in large doses. Under these conditions the red cells undergo marked changes in shape and color (Hayem). The fats and lecithin are dissolved, and the hemoglobin becomes dissociated from the stroma and precipitated in reddish, refractile droplets. Bordet and Massart showed alcohol to have a strong negative chemotactic influence on the white blood-cells, even when greatly diluted.

> Microscopic changes in the tissues as a result of alcohol, taken from observations on animals: 1. The most marked effects are produced on the blood-vessels. 2. The cells which line the vessels are swollen and broken, and there are serious retrograde changes in all of the tissues. The white blood-cells become swollen and necrotic. 3. The lymph-spaces become choked with broken-down white blood-cells, and the small blood-vessels are also completely blocked by plugs in detritus and dead tissue. 4. In the veins the blocking is often so severe that the vessels burst from the backing up of blood in them. The changes are always more marked in the vessels of the brain than elsewhere because they do not possess the special nerves which control their caliber, as do the vessels of other parts of the body. H. J. Berkley (Johns Hopkins Hosp. Bull.; Amer. Jour. of Physiol. Therap., May, 1910).

Respiration.—Volumetric estimations made before and after the ingestion of alcohol have shown fairly conclusively that, even in the absence of motor excitement, the drug causes an increase in the amount of air breathed. Usually the augmentation is more pronounced in fatigued or exhausted individuals. Considerable experimentation has been indulged in for the purpose of ascertaining whether the drug stimulates directly the respiratory centers in the medulla or whether the effect is of indirect origin, viz., through irritation of the gastric mucosa. Thus Loewy conducted experiments in which the irritability of the centers of respiration before and after the use of alcohol was ascertained through its response to an increase of carbon dioxide in the blood. The results of these and other researches have not been entirely conclusive, but, in a general way, they tend to show that alcohol exerts, in man at least, little if any direct central stimulation, and therefore, that the improvement in respiration observed under the influence of therapeutic doses of alcohol is probably due to a reflex effect on the centers. An additional argument in favor of the latter view is in the fact that respiratory depression occurs only under exceedingly large doses of alcohol and at a late stage in the poisoning, tending to show that the effect of this drug on the respiratory centers is, under ordinary circumstances, not a very

marked one. Yet it is well known that in the final stage of acute alcoholic poisoning the breathing becomes more and more shallow and infrequent, complete arrest ultimately occurring.

In fever, both the respiration and the heart-rate are slowed by alcohol. This seems reasonably accounted for by a lessening of general bodily excitement through the narcotic action of alcohol, without implicating a direct depressing action of moderate doses of it upon both the respiratory centers and heart.

Secretions.—Many of the secretions are to a certain extent activated by alcohol. The saliva and digestive secretions are increased reflexly by the local action of alcohol on the mucous membranes, as well as, probably, after its absorption, through direct contact of alcohol with the gland-cells as the drug circulates with the blood-stream. The sweat secretion is increased owing to the peripheral vasodilatation. The urine is also augmented. The question whether a direct exciting action on the renal epithelium is exerted or not has not yet been settled, though the fact that albuminuria may result from excessive doses would seem to point to an irritative effect on the kidney cells.

Temperature.—Alcohol in ordinary doses causes a slight fall in the body temperature (¼° to 1° C., according to Cushny), owing to the dilatation of the superficial blood-vessels, which exposes a larger amount of blood to the cooling influence of the surrounding air. At the same time a sensation of warmth is experienced, and the temperature of the skin may rise considerably owing to its flushed condition. If a large amount of alcohol be taken the fall of internal temperature may be exaggerated owing to the complete motor inactivity. The same will occur under a moderate dose of alcohol if the subject be subsequently exposed to cold.

Metabolism.—Alcohol causes but little change in the oxygen intake and carbon dioxide output, which, after its ingestion, show no modification beyond that to be expected from any other substance yielding energy to the system by oxidation. Of course, if alcohol be taken in amounts sufficient to produce sleep, the respiratory gaseous interchanges will be lowered because of the muscular inactivity. Where the drug is taken repeatedly in moderation, however, a gradual increase in the oxidizing power of the blood occurs, apparently corresponding in amount to the degree to which tolerance of alcohol has been developed in the individual. This fact was well illustrated in the experiments of Hunt on the toxicity of methyl cyanide, a compound whose poisonous effect is proportional to the extent to which it is oxidized to hydrocyanic acid in the system. Animals given repeated small doses of alcohol, insufficient in themselves to elicit signs of intoxication, showed an increased susceptibility to methyl cyanide, demonstrating that the oxidizing power of the blood had become greater.

In addition, the administration of alcohol, which is almost entirely destroyed in the system by oxidation, naturally tends to preserve from combustion other oxidizable substances present—fats in particular. This accounts for the well-known fattening tendency of alcoholic beverages, when habitually taken in any but very moderate amounts (see section on Alcohol in Nutrition).

Immunity.—As to the influence of alcohol on the powers of resistance of the individual to disease, it is well known that alcoholics are less

resistant to acute infections and more susceptible to dangerous shock from bodily injury than are the temperate. Likewise, animals given alcohol and subsequently inoculated with pathogenic organisms or injected with disease toxins have always shown a low degree of resistance as compared to normal animals. Delearde and Laitinen in their experiments found it "almost impossible to confer immunity against rabies, tetanus, and anthrax on alcoholized animals." The question, however, whether alcohol in the amounts in which it has been used in the treatment of acute febrile diseases in non-alcoholics has a similar prejudicial effect has not been definitely settled.

[Inasmuch as the defensive power of the body fluctuates with its vital activity, beverages rich in alcohol, besides inhibiting the life process itself, place it at the mercy of disease-breeding germs, and thus actually help to destroy life through deoxidizing or reducing action on the blood.

This is further emphasized by the influence of alcohol on the ductless glands themselves. While small doses or weak solutions, as stated by Lorand, stimulate these organs, large quantities of beverages strong in alcohol cause their degeneration, as shown by numerous autopsies. My work on the "Internal Secretions" contains a microphotograph showing a pituitary body in which alcohol produced sclerosis. Hertoghe and de Quervain have found alcohol harmful to the thyroid—an organ which, as is well shown by cretinism and the marvelous effects of thyroid preparations in this disease, has much to do with the development of the body. The defensive functions of the body, if carried on, as I hold, by the ductless glands, are thus directly hampered by the use of alcohol in any but very weak solutions. This coincides with the recent observations of Parkinson, who studied the influence of alcohol on the autoprotective functions of the body. While his experiments showed that small quantities temporarily enhanced the production of antibodies, as soon as they were replaced by large doses the opsonic index fell; and if their use was continued, it remained low permanently, which meant that the immunizing functions were paralyzed. This confirmed the earlier experiments of Müller, Wirgin, and others referred to below.

It is because of this fact that drunkards in general fare so badly in infectious diseases; their autoprotective mechanism is powerless to defend them. Quite in accord with these teachings of experience, Parkinson found that the reaction to vaccines was much less effective in alcoholized rabbits than in normal rabbits, and that the difference was still more marked when living micro-organisms were used. Many experiments by competent observers afford evidence in the same direction. Again, I have shown that the immunizing process of the body is closely linked and runs on parallel lines with oxidation; since alcohol in anything but small doses reduces oxidation, it inhibits in proportion our power to fight disease during the active or defensive phase of the morbid process, especially in febrile infections and toxemias.

If alcohol is used at all, therefore, in the acute infections and toxemias, it should only be given in small quantities and freely diluted. But better agents to enhance the defensive process are now available. C. E. DE M. S.]

Friedberger, Müller, Wirgin, and other observers found that, in rabbits, the administration of alcohol for some days in amounts sufficient to produce a mild degree of intoxication interferes with the formation of antibodies in the blood. The greater the time allowed to elapse, however, between the injection of the antigen and the giving of alcohol, the less the restraining effect of the latter on the development of protective substances. Experiments conducted by Laitinen, in which animals were given for some time doses of alcohol so small as to correspond with the amounts taken dietetically by moderate users of

alcohol, did not reveal any pronounced disadvantage in the habitual use of small quantities of alcohol as regards susceptibility to disease, the mortality being but slightly greater than among the animals not given alcohol.

Alcohol in small quantities has no action on the phagocytic activity, nor has it any action on the phagocytic activity until it is present in 12.5 per cent. strength. Small quantities of alcohol injected into rabbits may stimulate the production of antibodies temporarily. A large dose lowers the opsonic index for twenty-four hours. Continuous moderate doses cause a permanent lowering of the opsonic index. The reacting mechanism to vaccines is much less effective in alcoholized rabbits than in normal rabbits; the difference is still more marked when living micro-organisms are used. P. R. Parkinson (Lancet, Nov. 27, 1909).

Ingestion of alcohol is quickly accompanied by a lowered opsonic index, but the index as quickly returns to the normal with cessation of the alcohol. The amount of alcohol needed to bring about this result had no influence on the resistance of the animal to infection. Abbott and Gildersleeve (Univ. of Penna. Med. Bull., June, 1910).

Study of protein metabolism and utilization, and especially the partition of nitrogen in the urine, under the influence of alcohol, carried out on man and dogs under fixed and comparable conditions of diet. There is no pronounced disturbance in the alimentary utilization of the foodstuffs. Moderate doses exert a protein-sparing action, which is succeeded by loss of nitrogen when larger quantities of alcohol are administered. The partition of urinary nitrogen remains remarkably unaltered, with the exception of an increased elimination of ammonia nitrogen and a higher output of purins. The most significant impression afforded was the absence of pronounced alterations indicative of markedly disturbed protein metabolism, even when comparatively large doses were continued for days and weeks. Mendel and Hilditch (Amer. Jour. of Physiol., Nov., 1910).

[As is the case with all food accessories, coffee, tea, pepper, common salt, etc., alcohol becomes toxic when used immoderately, and when insufficiently diluted. Light wines, beer, and other beverages that contain a very small proportion of alcohol, when taken in moderation, tend to activate the functions of the ductless glands, and, therefore, the autoprotective functions of the body. The harmful influence of alcohol begins as soon as the proportion of absolute alcohol in a beverage exceeds 5 per cent. to any marked degree, the toxic effects being due mainly to its property of becoming oxidized at the expense of the blood and other body fluids and cellular elements. When the proportion exceeds 10 per cent. and approximates that of brandy, whisky, and many patent or proprietary nostrums, alcohol becomes an active toxic; it tends to paralyze the functions of the ductless glands, and, therefore, the autoprotective functions, thus giving free sway to pathogenic germs, their toxins and other toxics, venoms, toxic wastes, etc., that may be present in the blood, thus defeating indirectly and insidiously the efforts of the physician. C. E. DE M. S.]

Absorption and Elimination.—The absorption of alcohol is very rapid, unless it be so concentrated as to coagulate the albumins with which it comes in contact. Roughly, 20 per cent. of alcohol ingested is absorbed from the stomach, and the remaining 80 per cent. from the intestine. Proceeding to the liver with the portal blood, it is in part arrested in this organ, the other portion passing through to enter the general blood-stream. Eventually much of the latter portion leaves the capillaries by exosmosis and is absorbed by the various tissues. The liver and brain have a special affinity for alcohol, the

former fixing four times and the latter twice as much as is present in the blood (Pouchet). More than 98 per cent. of the whole amount ingested is oxidized in the tissues (Atwater). The remainder passes out with the urine unaltered, though traces may still remain in the blood after the first twenty-four hours. The aroma of the breath of alcohol users is due rather to higher alcohols and by-products eliminated in this manner than to ethyl alcohol (Cushny). According to Brauer, some alcohol is excreted with the bile, then reabsorbed from the intestinal tract. An insignificant amount may leave the body with the sweat and milk. The products of the oxidation of alcohol in the system are believed to be acetic acid, carbon dioxide, and water. According to the researches of Dujardin-Beaumetz and Jaillet, it is oxidized in the red cells themselves, with the formation first of acetates of the alkali metals, then of carbonates. When the oxidizing capacity of the blood-cells is exhausted alcohol begins to be eliminated in large amount with the emunctories and to accumulate in the tissues.

Rôle of Alcohol in Nutrition.—The painstaking experiments of Neumann, of Atwater and Benedict, and of Rosemann have shown alcohol to be capable of sparing the fats and carbohydrates of the body through its combustion in their stead, *i.e.,* where the amounts of fat and carbohydrates ingested are insufficient for the needs of the body alcohol will, to a certain extent, act as a substitute, and prevent the remaining reserve of these substances in the system from being exhausted. The combustion of alcohol, however, yields but a comparatively small amount of heat, the body temperature being, therefore, seldom raised by it, but rather lowered, owing to the peripheral vasodilatation it also produces, with the consequent increase in heat loss. Neumann concluded from his experiments that alcohol could take the place of a chemically equivalent quantity of fat in the diet, and also that alcohol given in combination with a diet in itself sufficient would bring about an economy of proteins—as measured by the nitrogen excretion in the urine—in the same way that an extra amount of fat would. When moderate amounts of alcohol are taken, the first result is an increase in the amount of nitrogen excreted, which persists, as in the case of any other change in the non-nitrogenous constituents of the food, until the organism has become used to the new diet, *i.e.,* through a period of three or four days. After this the protein-saving property of alcohol asserts itself, the amount of urea and uric acid, as well as of sulphates and phosphates, eliminated with the urine showing a decrease. According to Pouchet, however, the proteins are spared by alcohol only if the subject is receiving in the diet an amount of protein in excess of the needs of the body at the time. If not, or in any case if the administration of alcohol be long enough continued, the amount of nitrogenous wastes will soon show an increase until the utilization of the body proteins becomes greater than normally—a condition of affairs unfavorable to the nutrition of the body. The same result will obtain at once where excessive, instead of moderate, doses of alcohol are used, the drug acting as a spur to the breaking down of the albumins.

It is possible to prolong the life of starving rabbits by the subcutaneous injection of suitable doses of alcohol, but larger quantities of alcohol hasten

the death of the animals. The favorable action of the alcohol is to be ascribed in part to its saving effect on albumin and the better preservation of the watery constituents of the organism. The acceleration of death under the influence of larger quantities is to be explained naturally by the increased destruction of albumin. A diuretic action is produced only by the administration of larger quantities of alcohol, smaller quantities having an opposite effect. Kochmann (Münch. med. Woch., Mar. 16, 1909).

The advantages of alcohol as a source of body energy may be said to lie in its ready absorption, the fact that no digestion of it is required, and that it is easily oxidized. In fever or conditions of central nervous exhaustion, with resulting temporary digestive failure, alcohol is, therefore, available for cautious use as a food. Roughly speaking, 4 minims of alcohol will yield the same amount of energy as 7 grains of sugar, starch, or protein or 3 grains of fat (Committee of Fifty, 1893).

The disadvantages of alcohol are that it has toxic side effects, that it leads to obesity, and, probably, that, even in the temperate, it tends to lower the resisting power of the body to disease.

M. Duclaux recently declared, on the strength of a number of experiments made on themselves by two American investigators (Atwater and Benedict), that alcohol, so far from being a poison, has, in moderate doses, a distinct dietetic value. This profession of faith, made, as it was, just at the time when the Académie de Médecine was, at the request of the Minister of the Interior, drawing up a list of toxic essences employed in the manufacture of liquors, and when the Prefect of the Seine had placarded the walls of Paris with warnings as to the deadliness of alcohol, caused no little scandal among the antialcohol party, who, with the charity characteristic of "antis" of every hue, even hinted that the opinion of the distinguished successor of Pasteur was not altogether disinterested. This ignoble imputation is mentioned only to show the degree of malevolence and mendacity to which the minds of well-meaning persons can be inflamed by prejudice. In La Revue, M. Duclaux states that no definite practical consequences can yet be drawn from the experiments of Atwater and Benedict. He is anxious that the question should be fully discussed, but he awaits the coming of adversaries who will consent to read and reflect before rushing into print. In the mean time he will agree to a truce, accepting as an average one liter of wine a day, an amount which has been shown by the American investigators to be harmless and even useful. The wine must be well diluted with water, and its consumption spread over a day.

Roux, also of the Pasteur Institute, holds that, even if Atwater and Benedict's experiments be accepted, the fight against alcohol must still be continued. He thinks that habitual drinkers will never submit to the restricted allowance which Atwater and Benedict imposed on themselves. In regard to wine, Roux admits that the experience of centuries as seen in whole nations shows that moderate drinking does no harm. Metchnikoff holds that alcohol in any form is a poison. He confesses, however, that he has not made a special study of the question, and his conclusion is based on his personal experience. He never drinks alcohol himself, as he has found that even a small quantity makes him giddy. Berthelot is clear that alcohol is not a food. In very small doses it may be useful as a medicine. He thinks alcoholism is a factor in the present decadence of most European nations, and that their only hope of salvation lies in vigorous legislation against the evil. Brouardel gives the guarded reply that from the chemical constitution of a body no conclusion can be drawn as to its alimentary value; experience alone can decide

the question. Charles Richet says there is no doubt that alcohol is a food, and that in very small doses, when pure, it is almost harmless. This fact, however, does not warrant the inference that it is a good food. He thinks that men must be angels before alcohol ceases to be a great danger. It is a mischievous delusion to think that alcohol is consumed as a food; it is rather its poisonous effects that are sought by unfortunates anxious to forget their misery. Professor Bernheim, of Nancy, does not think that the use of alcohol should be proscribed. He even holds that many abstainers from "the generous wine of France" are actuated by *snobisme*. Wine, he says, is, like other medicines, poisonous only in large doses. It would be as reasonable to forbid its use on that account as to condemn the eating of meat because it contains ptomaines, or eggs because phosphorus enters into their composition. Like everything that we take, wine suits some and not others.

Lancereaux also holds that wine is dangerous only if taken in too great quantity—for instance, in a daily quantity of 3 liters. Alcohol in every form, however, if taken to excess, brings on premature senility and tends directly to tuberculosis and death. Héricourt holds that, to the question, Is alcohol food? no absolute answer can be given. Every food is toxic in certain amounts, and, although the consumption of a liter of wine a day may have been a direct cause of the death of anyone, it may be so indirectly, as by diminishing the power of resistance to disease.

Dr. Landouzy is of the opinion that natural wine taken in doses suitable to age, constitution, and mode of life does not deserve the uncompromising condemnation of intemperate advocates of temperance; he looks upon spirits and liqueurs, however, as, generally speaking, pernicious. Magnan thinks that, whatever chemistry or experimental physiology may appear to show, alcohol can never be recommended as a food. Garnier, speaking from a large prison experience, says that alcohol is responsible for 70 per cent. of all the crimes committed in France. Bourneville is not hostile to wine; he holds, with Duclaux, that, from the hygienic point of view, it is distinctly useful in moderate doses.

On the whole, then, the weight of opinion among leading scientific men in France is in favor of the dietetic value of wine. But the wine must be pure and it must be taken in moderate amount. Those who, like Cassio and Metchnikoff, have very poor and unhappy brains for drinking ought, by all means, to avoid looking upon the wine when it is red. They have no right, however, to make this personal idiosyncrasy the measure of other people's tolerance, still less to found upon it a universal law for the governance of mankind.

As to the deadly effects of the abuse of alcohol we are all agreed, and probably all will also agree that its use should be carefully regulated in accordance with individual constitution. The experience of men differs. Gladstone, who had an "open mind" in most directions, tested the matter for himself. He found that wine helped him when he had to make an extraordinary oratorical effort, and the want of it made the effort more laborious and less successful. On the other hand, some find that wine paralyzes their faculties. In regard to alcohol, it may be said with truth that what is one man's meat is another man's poison, and that homely proverb seems to us to sum up the teachings of science and philosophy on the question. Editorial (Brit. Med. Jour., Mar. 14, 1903).

The following comparative table represents demonstrable facts and the teachings of laboratory work:—

Food.	Alcohol.
1. A certain quantity will produce a certain effect at first; the same quantity will always produce the same effect in the healthy body.	1. A certain quantity will produce a certain effect at first, but it requires more and more to produce the same effect when the drug is used habitually.

Food (*Continued*).	Alcohol (*Continued*).
2. The habitual use of food never induces an uncontrollable desire for it in ever-increasing amounts.	2. When used habitually it is likely to induce an uncontrollable desire for more, in ever-increasing amounts.
3. After its habitual use a sudden total abstinence never causes any derangements of the central nervous system.	3. After its habitual use a sudden total abstinence is likely to cause a serious derangement of the central nervous system.
4. Foods are oxidized slowly in the body.	4. Alcohol is oxidized rapidly in the body.
5. Foods, being useful, are stored in the body.	5. Alcohol, not being useful, is not stored in the body.
6. Foods are the products of constructive activity, activity of protoplasm in the presence of abundant oxygen.	6. Alcohol is a product of decomposition of food in the presence of abundant oxygen.
7. Foods (except meats) are formed in nature for the nourishment of living organisms, and are, therefore, inherently wholesome.	7. Alcohol is formed in nature only as an excretion. It is, therefore, in common with all excretions, inherently poisonous.
8. The regular ingestion of food is beneficial to the healthy body, but may be deleterious to the sick.	8. The regular ingestion of alcohol is deleterious to the healthy body, but may be beneficial to the sick (through its drug action).
9. The use of foods is followed by no reaction.	9. The use of alcohol, in common with narcotics in general, is followed by a reaction.
10. The use of food is followed by an increase in activity of the muscle-cells and brain-cells.	10. The use of alcohol is followed by a decrease in the activity of the muscle-cells and brain-cells.
11. The use of food is followed by an increase in the excretion of carbonic oxide.	11. The use of alcohol is followed by a decrease in the excretion of carbonic oxide.
12. The use of food may be followed by accumulation of fat, notwithstanding increased activity.	12. The use of alcohol is usually followed by an accumulation of fat through decreased activity.
13. The use of food is followed by a rise in body temperature.	13. The use of alcohol may be followed by a fall in body temperature.
14. The use of food strengthens and steadies the muscles.	14. The use of alcohol weakens and unsteadies the muscles.
Food (*Concluded*).	Alcohol (*Concluded*).
15. The use of food makes the brain more active and accurate.	15. The use of alcohol makes the brain less active and accurate.

[Alcohol is considered as a food-sparing agent by some observers, its value corresponding with its dynamic equivalent of pure food hydrocarbon. This presupposes, however, that alcohol is utilized by the tissues in the same manner as these hydrocarbons—merely because its oxidation liberates energy in the form of heat. But this is a fallacious conception; alcohol only simulates normal oxidations; far from being the product of cellular exchanges which constitute the vital process, the heat it liberates is at the expense of the tissue, since by becoming oxidized itself, especially in the liver—whereby the body is protected against its toxic effects—it utilizes oxygen intended to sustain tissue metabolism. If alcohol were a food, large doses would prove more profitable to the organism than small ones; but the reverse is the case; large doses inhibit all activities that would be enhanced by a liberal use of food. The debilitating action of alcohol on the nervous system, for example, has been demonstrated by Bunge, Schmiedeberg, Ach and Krepelin, and others, while Dogiel found that it depressed markedly both motor and sensory nerve-centers. It does this not only with nervous tissue, but with all tissues. A depressing agent cannot logically be regarded as a food. C. E. DE M. S.]

In healthy persons alcohol unquestionably plays the same rôle as a food, *e.g.*, a carbohydrate or a fat. In contrast to fats and carbohydrates, alcohol spares the proteids only in those cases in which the organism has become accustomed to the action of the stimulant, which usually takes several days. In disease alcohol apparently acts upon metabolism in the same way as in health. It is particularly useful as a food in diabetes mellitus; by taking the place of fats in the food it lessens the production of the acetone bodies. Hare showed that alcohol raises the power of the blood to destroy bacteria. Friedberger found that under the influence

of alcohol the blood acquired an increased resistance against the cholera vibrio. Mircoli found that under the influence of alcohol the body acquired the power to resist the tubercle bacillus. A. K. Sievert (Roussky Vratch, Oct. 24, 1909; N. Y. Med. Jour., Jan. 1, 1910).

[The protective influence of alcohol referred to here applies to small quantities only. Everyone knows and hospital experience has amply and conclusively shown that alcoholism greatly weakens the power of the body to resist disease. C. E. DE M. S.]

External Action.—Applied to the skin and allowed to evaporate, alcohol reduces the local temperature because of its marked volatility. It may also exert an anesthetic effect. If evaporation be prevented, however, and the contact maintained for some time, alcohol acts as an irritant. Owing to its rather high diffusion power, it penetrates through the cuticle to the underlying tissues, and induces a sensation of heat, often preceded by itching and accompanied by reddening of the skin surface. It may thus be employed as a counter-irritant. For such effects a concentration of about 60 per cent. or over is required, more dilute solutions not giving rise to distinctly irritative phenomena. When applied to ulcers and other open surfaces, alcohol may, through its irritant properties, hasten tissue repair. The prominent local effects of concentrated alcohol include the abstraction of water from the tissues, and the coagulation of albumin. It is because of these effects, and also by dissolving out the fat, that alcohol hardens the skin when repeatedly applied. It is sometimes used to cover sores or wounds with a thin, protective, air-excluding layer of coagulated albumin, which facilitates healing. Alcohol may also act as an astringent, a property not infrequently availed of in such condition as salivation, pharyngeal relaxation, scurvy, etc., alcoholic preparations being employed as mouth-washes and gargles. The irritant and astringent powers of alcohol are naturally more pronounced upon the mucous membranes and upon wound surfaces than upon the skin, and dilute preparations can, therefore, be used on the former to procure effects such as only concentrated ones would produce on the skin. Inhalation of the vapors of alcohol is capable of causing temporary spasm of the laryngeal muscles through reflex irritation. Alcohol has noteworthy antiseptic and germicidal properties, which may be utilized in the disinfection of wounds. According to Harrington and Walker, 60 and 70 per cent. alcoholic solutions, applied to wounded surfaces for at least five minutes, are the most efficient in destroying bacteria. In these percentages alcohol corresponds in strength to about 3 per cent. phenol (Cushny). Dry bacteria may not be destroyed by a day's exposure to absolute alcohol.

Against dry bacteria, absolute alcohol and ordinary commercial alcohol are wholly devoid of bactericidal power, even with twenty-four hours' direct contact, and other preparations of alcohol containing more than 70 per cent., by volume, are weak in this regard, according to their content of alcohol,—the stronger in alcohol, the weaker in action. Against the commoner, non-sporing, pathogenic bacteria in a moist condition, any strength of alcohol above 40 per cent., by volume, is effective within five minutes, and certain preparations within one minute. Alcohol of less than 40 per cent. strength is too slow in action or too uncertain in results against pathogenic bacteria, whether moist or dry. The most effective dilutions of alcohol against the strongly resist-

ant (non-sporing) bacteria, such as the pus organisms, in the dry state, are those containing from 60 to 70 per cent., by volume, which strengths are equally efficient against the same organisms in a moist condition. Unless the bacterial envelope contains a certain amount of moisture, it is impervious to strong alcohol; but dried bacteria, when brought into contact with diluted alcohol containing from 30 to 60 per cent. of water by volume, will absorb the necessary amount of water therefrom very quickly, and then the alcohol itself can reach the cell protoplasm and destroy it. The stronger preparations of alcohol possess no advantage over 60 to 70 per cent. preparations, even when the bacteria are moist; therefore, and since they are inert against dry bacteria, they should not be employed at all as a means of securing an aseptic condition of the skin. Provided the skin bacteria in the deeper parts can be brought into contact with disinfectants, alcohol of from 60 to 70 per cent. strength may be depended upon usually, but not always, to destroy them within five minutes. Charles Harrington and Harold Walker (Boston Med. and Surg. Jour., May 21, 1903).

THERAPEUTICS.—As a "Stimulant."—The opinion of the medical profession in regard to the value of alcohol as a stimulant is divided, and the extent to which the drug is employed in the treatment of disease (exception being made of its external uses) is on the decline.

The more recent studies have brought out the importance of the vasodilator influence of alcohol, and cast a shadow on its effectiveness as a true stimulant. By many it is believed that a part, if not all, of the stimulating effect of alcohol results from the local irritation produced by it in the stomach, the centers in the medulla oblongata being thereby excited reflexly.

[Buchner, Chittenden, Mendel, Jackson, and many other authorities have shown that beverages which contain a small proportion, about 5 per cent., of absolute alcohol, such as light wines, beer, etc., increased the production of gastric juice and the activity of the digestive process. Being entirely oxidized in the stomach and promptly eliminated by the lungs and kidneys, this small percentage, unless taken in large quantities, does not influence morbidly either the blood or its oxidizing body. Such is not the case, however, when the proportion of absolute alcohol exceeds 5 per cent. to any marked degree. A beverage containing 10 per cent., for example, retards digestion manifestly, and if stronger, as is the case with brandy, whisky, etc., it tends besides, as first shown by Claude Bernard, to cause coagulation of the gastric secretion and its ferments. Under these conditions, the functions of the digestive tract are not alone interfered with, but considerable alcohol is absorbed into the blood. It is this absorbed alcohol which does incalculable harm. Being oxidized at the expense of the blood's oxidizing body—of adrenal origin—it robs the tissues of that which sustains their life. C. E. DE M. S.]

Partly because of the fact that it is often the only remedial agent immediately available, it is still largely administered, especially by the laity, in all varieties of emergencies. Its effect, though of short duration, is exerted promptly.

As a cardiac and respiratory stimulant alcohol is made use of in immediately dangerous conditions, such as **syncope, shock, collapse,** severe **hemorrhage, asphyxia,** and **poisoning by depressant drugs,** as well as, in many instances, in the course of acute infectious diseases, such as **typhoid fever, typhus, pneumonia, diphtheria, small-pox, scarlatina, septicemia, erysipelas, tetanus, yellow fever, cholera, dysentery, influenza,** etc. The consensus of present opinion is that alcohol should never be administered

continuously, even in severe infections, but should be reserved for periods of unusual depression, when special stimulation is necessary to tide the patient over a dangerous crisis. In selecting the dose to be used, the vasodilator influence of alcohol must always be remembered, excessive doses tending to lower markedly the tone of the blood-vessels,—the importance of which tone in the maintenance of cardiac activity is well recognized. According to many, indeed, the use of alcohol in shock is to be avoided, as this is a condition of paretic vasodilation, and the vasodilator effect of alcohol exerted after its absorption is likely to prove more harmful than its primary reflex stimulating effect on the heart and respiration will have done good. Similarly in severe hemorrhage, alcohol has been said to be contraindicated, owing to its vasodilator property.

> While alcohol may stimulate the heart and raise arterial pressure momentarily, its secondary effect is that of a cardiac depressant and a vasodilator. The only time when alcohol is a stimulant is in acute **cardiac failure,** and then it is stimulant to the heart only before its absorption, reflexly from the irritation, when taken in concentrated solution, of the mucous membrane of the mouth, pharynx, esophagus, and stomach, the rectum, if it is administered as an enema, and the tissues, if it is given hypodermically. To obtain such stimulation the alcohol must be in strong preparation—either brandy, whisky, gin, rum, or champagne. This reflex irritation through the vasomotor center temporarily raises the blood-pressure, and perhaps, through the accelerator nerves, stimulates the heart. To keep up this stimulation another dose must soon be given, in from fifteen minutes to half an hour or an hour, depending on the prolongation of the heart weakness. The dose of alcohol for such stimulation should be small in order that the results from the subsequent absorption will be the minimum, as the vasodilator effects are not desired. If the alcohol is administered too frequently it accumulates in the system before the previous doses can be burned or eliminated, and then to obtain stimulation it will be necessary to give a larger, concentrated dose to cause sufficient irritation and stimulation to overcome the depression of the previous doses. Soon the vasodilation is increased, the heart is depressed, the nervous system more or less paralyzed, and depression is added to depression. Consequently, the only excuse for using alcohol in any form as a cardiac or circulatory stimulant is when the depression or syncope is short-lived, or, perhaps, as a primary stimulant in acute collapse. (Jour. Amer. Med. Assoc., Nov. 6, 1909.)
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> Observations on the remarkable stimulant effect on the heart and circulatory system produced by the inhalation of oxygen containing alcohol vapor. There are the good effects of the oxygen plus an additional marked stimulant effect on the circulation caused by the contained alcohol vapor. Oxygen which had been bubbled through absolute alcohol contained in an ordinary wash-bottle was administered in several cases of illness in which **cardiac failure** was a prominent symptom, and it was found that the mixture produced a marked stimulant effect on the heart and circulation, decidedly greater than that produced by oxygen alone. In some of these cases the administration appeared to have been the cause of prolongation and saving of life. In cases of pneumonia with cardiac failure the mixture of oxygen and alcohol vapor was found to be a valuable remedy. Willcox and Collingwood (Brit. Med. Jour., Nov. 5, 1910).

In emergency conditions, large doses of alcohol, *e.g.*, 1 or 2 ounces (30 to 60 c.c.) of whisky or brandy, are not infrequently administered. Where, owing

to unconsciousness or profound adynamia, the spirits cannot be swallowed, they may be injected subcutaneously. By this method absorption of the drug is more rapid, and its general effect correspondingly hastened. Alcohol may also be given by rectum, preferably in the form of brandy.

In the treatment of **wounds** inflicted by **venomous snakes** and **poisonous fishes**, the internal use of alcohol has long been considered an effective measure, though the idea that the drug exerts a specific antidotal effect in these cases appears to be based on pure assumption. Large doses are customarily given in these cases, but this should certainly not be pushed to the point of adding an acute alcoholic intoxication to the difficulties with which the system already has to contend.

In the prostration attending cases of **meat poisoning** or **ergotism**, the administration of alcohol also often proves valuable.

As a Vasodilator.—The value of alcohol in feverish or frankly febrile conditions depends in reality on not a single, but a group, of effects, which have been enumerated by Sollmann as follows: 1. Dilatation of the cutaneous vessels. 2. Counteraction of the nervous phenomena of fever, through narcotic action. 3. The furnishing of a readily absorbable food. 4. Diuresis. Among these effects peripheral vasodilation ranks as the most important. When the pulse becomes of the high-tension variety, owing to excitation of the contractile vascular walls by disease toxins, and the superficial circulation becomes sluggish, for the same reason, alcohol is likely to prove beneficial by dilating the vessels, lowering the tension, facilitating the work of the heart, and promoting perspiration. It will act thus pre-eminently as a restorer of the circulatory equilibrium. Certain particular indications for the use of alcohol in fevers have been formulated, viz., where in addition to a frequent, small, or irregular pulse or respiratory depression there are present dryness of the tongue and skin, together with restlessness and delirium or, on the other hand, indifference and hebetude, and perhaps subsultus tendinum,—phenomena commonly grouped under the term "**typhoid state.**" While, in a general way, the validity of these indications for alcohol seems to be established upon the basis of past experience, it cannot be said that the drug will invariably be productive of benefit where the indications are present. If, alcohol having been administered, the pulse and respiration are improved, the mouth and skin rendered moist, and the mental condition corrected, the propriety of employing it in the individual case will become apparent.

> As a vasodilator in chronic high arterial tension alcohol should ordinarily not be used. This indication is present in arteriosclerosis and gout, and is a symptom and sign in late middle life or old age. If the condition requires treatment it is much better managed by nitroglycerin, thyroid extract, potassium iodide, or small doses of chloral. If arteriosclerosis is present and the patient is well along in life and is accustomed and has been accustomed to take alcohol regularly in doses that do not intoxicate, it may be unwise to stop the vasodilating effects of the alcohol until it has been ascertained that some other treatment will be as conducive to his well-being. In other words, the physiological relief from high tension which he has been accustomed to acquire by taking alcohol cannot be abruptly stopped without due consideration of the consequences of withdrawing the drug. (Jour. Amer. Med. Assoc., Nov. 6, 1909.)

The dose of alcohol given in the **febrile diseases** has usually been that represented by ½ to 1 ounce (15 to 30 c.c.) of whisky or brandy, diluted with water, this amount being repeated every two to four hours. While it has been a matter of common observation that very large doses of alcohol may be given in fever without eliciting the ordinary signs of intoxication, this fact should not be interpreted as giving the physician license to introduce alcohol into the systems of patients without due consideration of the dosage. It should be kept in mind that alcohol, though setting free energy in the form of heat through its oxidation, in doing so draws upon the supply of oxygen present in the tissues, and if caused to accumulate in the system through injudicious dosage is likely seriously to interfere with other oxidative processes essential to the welfare of the economy. Hence the tendency recently has been, if alcohol is used at all in fever, to limit strictly the amount given to what is necessary for amelioration of the symptoms.

According to Osborne, a dose larger than 1 to 3 teaspoonfuls, once every three hours, is probably never indicated in febrile conditions; if this dosage be exceeded, the harmful effects resulting when alcohol is given in amounts that overtax the oxidizing powers of the tissues and lead to accumulation of the drug in the system will be avoided. Butler counsels that, even in cases where alcohol proves beneficial, it should rarely be given throughout the twenty-four hours, but reserved for periods when the heart action grows especially weak, usually in the interval between midnight and 7A.M. One fluid-ounce (30 c.c.) of whisky may be given before midnight and repeated every three hours. In lieu of pure whisky or brandy, diluted alcohol may also be advantageously given in the form of milk punch or eggnog.

> In infectious diseases alcohol should never be given unless the patient is near collapse. Even in small doses it weakens the resistance, and so favors the action of the invading microbe. It is a cause of stillborn infants, with more or less widespread fatty degeneration. Gruber (Wiener klin. Woch., May 9, 1901).
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> The effect of alcohol on the circulation in the sick, and its effect on the power of man's blood to resist infection, studied experimentally. Only the results of study of the first of these two problems are now reported. The following facts, regarding the action of alcohol, the author considers as already established by the investigations of many observers: (*a*) In health alcohol can replace the fats and carbohydrates. Whether it can replace the proteids is not yet settled. Alcohol is both a food and a poison. (*b*) In the stomach alcohol disturbs the digestive process to a greater or less degree. After absorption it exerts through the nervous system a temporary increase both in the secretion and in the motility of the stomach. On intestinal absorption, so far as known, alcohol exerts little or no influence. (*c*) In healthy people and in persons with cardiac and renal diseases alcohol has no considerable diuretic power. In healthy people it rather decreases than increases diaphoresis. (*d*) The labor of respiration is increased by alcohol, yet there is no increase in the amount of O absorbed, nor in the quantity of CO_2 given off. To the above facts regarding the action of alcohol the writer adds the following, ascertained experimentally: 1. The action of alcohol upon the circulation is *nil.* Neither the maximum nor minimum blood-pressure showed any variation that could reasonably be attributed to the action of alcohol. 2. From the study of 309 patients suffering from a great

variety of diseases it would seem that alcohol, in therapeutic doses, has no effect on the temperature, pulse rate, respiration rate, appetite, delirium, and secretions. These observations should not, however, be interpreted as proving that alcohol is useless or useful in disease. R. C. Cabot (Boston Med. and Surg. Jour., July 23, 1903).

Rabbits injected with diphtheria toxin or other infectious products, followed by injection of alcohol, the results confirming the clinical observations of Dennig, Hindelang, and Grünbaum in respect to the injurious action of alcohol on the circulation during febrile conditions. The alcohol improves the respiration, but this favorable effect is outbalanced by its unfavorable action on the circulation, the blood-pressure dropping and the amplitude growing smaller, although the pulse rate may remain the same. It is necessary to restrict the use of alcohol in febrile states, weighing in each individual case whether the euphoria that follows the use of alcohol outbalances the inevitable somatic injury. Alexandroff (Corresp.-Blatt f. schweizer Aerzte, May 20, 1910).

Impairment of the vascular regulating mechanism is more apparent than active disturbance of the heart in the circulatory derangements of the acute infections. Treatment should, therefore, be directed to the prevention or correction of these vasomotor disturbances, and, while alcohol in small doses sometimes acts as a cardiovascular stimulant, its mode of action is not quite clear. In larger amounts, in individuals not accustomed to its use, it invariably acts as a depressant, paralyzing the vasomotor center. The border line between doses that act as a stimulant and those which act as a depressant is very uncertain. Some investigators have been unable to detect a rise in blood-pressure, even with very moderate doses, and this uncertainty renders it an undesirable therapeutic agent. Even in small doses it may, and in large doses always, depress the circulation, and other drugs more constant in their action are advisable, being less likely to affect the patient unfavorably. J. L. Miller (Jour. Amer. Med. Assoc., Dec. 10, 1910).

Alcohol is frequently used to increase the warmth of the body surface in the presence of chilly sensations or after exposure to cold. This is accomplished through the peripheral vasodilation which it produces. It must not be forgotten, in this connection, that peripheral vasodilation results in increased heat loss; if, *during* exposure to cold, peripheral vasodilation be produced and maintained for some time, as by repeated ingestion of alcohol, the result cannot but be an excessive loss of body heat, with merely temporary relief, and ultimate lessening of the resisting powers. Hence alcohol to warm the body surface should only be given *after* exposure or just before the period of exposure is to terminate.

In the initial stage of colds and of acute catarrhal inflammations of the respiratory passages in general, alcoholic preparations have been much used with the idea that by sharply activating the circulation of blood at the periphery local congestions will be relieved and the cold thus aborted. The patient takes a good-sized dose of whisky, followed by smaller doses every three or four hours, and stays in bed for a day, to facilitate the re-establishment of the circulatory equilibrium. While there is no doubt that alcohol, in combination with external warmth, will often bring about the desired result, the same effect can be procured by means of a hot bath, a coal-tar drug, and a saline purgative, without resorting to the use of alcohol.

In arteriosclerosis alcohol will act as a vasodilator and doubtless frequently performs this office in elderly individuals

accustomed to its use, but it should never be prescribed as such by the physician.

Where the **eruption** is **delayed** in the acute exanthematous diseases, a dose of whisky, taken hot, may bring about its early appearance.

As a Narcotic and Hypnotic.—The slightly depressing action of moderate doses of alcohol on the cerebral functions is a contributing factor in its usefulness in febrile conditions. Mild **delirium** will be relieved by it, or if no delirium be present the oncoming of sleep will be favored. The narcotic action of alcohol, however, is only of secondary importance, and should not be utilized unless there are other indications for the use of the drug. In febrile states a part of the quieting effect on the brain is due to a lowering of the tension in the cerebral circulation through the general vasodilation which the drug produces.

In mild degrees of **insomnia** in the aged, a little alcohol taken before retiring will promote sleep. But it is preferable to use other remedies; thus where the insomnia, as is often the case, is due to high blood-pressure, nitroglycerin should be substituted for alcohol, as a vasodilator. A mixture of equal parts of hot milk and of good ale or beer has been recommended as a promoter of sleep.

> Although alcohol in proper dose and in the proper form has an hypnotic effect not only by dilating the peripheral vessels and relieving the tension of the cerebral circulation, but also by its quieting effect o the nervous system, it should not frequently be considered or used as a **hypnotic.** Still, instances occur both in acute illness and in debilitated patients where it seems to be the safest and the most satisfactory of hypnotics. Of course, when alcohol is used thus as a drug it should be stopped by the physician as soon as he considers that the patient can tolerate another hypnotic, or that the positive indication has ceased to exist. In very old people who cannot sleep, alcohol as a "night-cap" has been frequently advised. Sleeplessness in senility is frequently due to high-tension circulation, and one can often cause these patients to sleep as well with small doses of nitroglycerin, administered at bedtime, as by alcohol so administered. (Jour. Amer. Med. Assoc., Nov. 6, 1909.)

Similarly, in insomnia in greatly weakened individuals, where alcohol may seem, for a time, the best hypnotic to use, other drugs should be substituted for it as soon as the patient's general condition permits. Beer or well-diluted spirits are most effective where the hypnotic action of alcohol is desired.

In **neuralgia** as well as **melancholia** and other forms of mental distress alcohol has given relief through its narcotic effect, but the danger of inducing chronic alcoholism in these cases is such that it is questionable whether it should ever be employed.

As a Stomachic, Antemetic, etc.—Ingested before or during meals, alcoholic preparations will frequently exert a pronounced beneficial effect in cases of **atonic dyspepsia** or in **anorexia** or poor digestion due to physical or mental **fatigue, acute illness,** etc. A small amount of wine or beer, or a little brandy diluted with water, by exerting a mild stimulating effect locally improves the gastric circulation and thereby promotes the secretory activity where this is deficient. The psychic effect of the odor and taste of wine, when agreeable to the patient, probably also plays a not inconsiderable part in improving the appetite. Dry wines should be given the preference in these cases, the sugar of sweet wines being detrimental,

Where anorexia is very marked, bitter tonics, such as calumba or quassia, in the form of tinctures or gentian or cinchona, in the compound mixtures, may be given in addition.

In certain forms of indigestion, alcohol does more harm than good, *e.g.*, where there is hyperacidity, or where the gastric mucosa is acutely inflamed. In all cases, moreover, where the necessity for gastric stimulation is likely to persist, *e.g.*, in the chronically debilitated and in the neurotic, the use of alcohol as a stomachic and stimulant to digestion is to be entered upon only with extreme caution, lest chronic alcoholism be the final result. This danger is less to be feared in the aged than it is in the young or middle-aged.

In **vomiting**, *e.g.*, in **seasickness** and in the **vomiting of pregnancy**, alcohol, especially in the form of champagne, sometimes proves helpful. A little brandy may be given on cracked ice in these disturbances, but champagne is decidedly the most effective preparation, combining the local anesthetic property of alcohol with the sedative action of carbon dioxide gas. In a somewhat similar manner, the **pain resulting from flatulence**, as well as **gastralgia**, may be relieved by the use of brandy (Butler).

In **diarrhea**, brandy is generally believed to exert a favorable influence, though the reason for its beneficial effect is not known. Red wines, by virtue of their tannin content, also tend to counteract diarrhea,—especially Bordeaux, dark Burgundy, and currant wine.

In conditions of **general debility** and during **convalescence** from exhausting diseases, even in the absence of gastric symptoms, alcoholic preparations are frequently given as general stimulants and reconstructives. The benefit produced results in part, doubtless, from activation of the digestive processes, but the food value of the preparations used, generally rich red wines, such as port and Madeira, or else beer, ale, porter, brown stout, and malt extracts, because of the additional nutritive substances they contain, must also be given due credit. To these favorable influences may be added the tendency to sleep and rest as a result of the narcotic action of alcohol, the improved distribution of blood through peripheral vasodilatation, the lessened resistance to cardiac action offered by the vessels, and the euphoria of the primary stage of alcoholic action. In severe cases of **diabetes mellitus** alcohol has also been used as a food.

Use of alcohol as a food in cases of severe **diabetes.** For years its value in such cases has been known clinically. But until recently we did not know whether the action was pharmacological or whether it was nutritive. In 1906, Benedict and Török, in studying the origin of acetone bodies in diabetes, substituted the fat of the dietary by alcohol and found a marked decrease in the output of acetone, sugar, and nitrogen. The sugar alone decreased 18 per cent. In severe cases with high ammonia the output was greatly decreased. Their work added further evidence of the protein-sparing action of alcohol. Neubauer, simultaneously, found alcohol of great service in severe diabetes. He used a wine containing 10 per cent. alcohol, allowing daily 12 to 24 ounces, equivalent to 450 to 900 calories of energy. He found regularly in severe cases a marked reduction in the output of sugar, acetone, oxybutyric acid, and ammonia. The total nitrogen and the amount of urine were decreased. In light cases of this disease, alcohol was of much less importance, but in severe diabetes, where the tissues cannot utilize carbohydrates, where only a little or no fat is allowable, and where protein alone tends to aggravate the

conditions, alcohol finds an invaluable place in the dietary. Aside from its action in diabetes and a few conditions of malnutrition, there has been no evidence produced thus far that alcohol is a better food than the sugars and starches. There is some reason to believe it somewhat inferior to them. There is abundant evidence that, on account of its habit-producing power and its baneful effects when used in excess, it should be condemned as food for healthy, normal individuals. Scarbrough (Yale Med. Jour., Feb., 1910).

As a Diuretic.—Dilute gin, light acid white wines, and light beers are the most strongly diuretic preparations of alcohol. This property can, however, only be considered as a relatively unimportant adjunct to the other actions of alcohol.

In Phenol Poisoning.—The value of alcohol in phenol poisoning has been shown to be due to the ready solubility of the phenol in it, the local action of phenol in concentrated form being thereby hindered. It is to be observed that this very dilution of the phenol is likely to hasten its absorption into the general system. Hence after giving the alcohol—preferably dilute—the physician should see that the stomach is emptied as soon as practicable.

External Uses.—Applied locally, alcohol has antiseptic, anesthetic, cooling, stimulating, solvent, astringent, dehydrating, and hemostatic properties. It is, therefore, a valuable agent in the treatment of **wounds**, especially **infected wounds**, in the management of which whisky, undiluted or diluted in the proportion of 1 to 4 of water, may be employed with advantage. In **snake-bites** concentrated alcohol mixed with ammonia may be used as a lotion after the poison has been sucked out; it is similarly useful in insect stings. In **puerperal sepsis** 50 per cent. alcohol has been used as an intra-uterine douche, and in 25 to 50 per cent. strength as a packing; better agents are, however, at our disposal.

For the treatment of **sprains, inflamed joints, contusions, strained muscles and tendons, headache, neuritis, abscesses, slight burns, erythema,** and **erysipelas**, alcoholic evaporating lotions are extensively used. A lotion composed of alcohol 8 parts, ammonium chloride 1 part, vinegar or dilute acetic acid 4 parts, in water 64 parts, will be found generally serviceable. Where a greater degree of absorption is desired, a gauze pad may be moistened with alcohol, applied over the involved area, and covered with rubber tissue. In **phlegmonous inflammations**, Salzwedel cleanses the part with ether, applies thick layers of cotton saturated with 90 per cent. alcohol, and covers the whole with an impermeable material, perforated in such manner as to delay, but not entirely prevent, evaporation. By this plan, he states, fever is lowered and the suppurative process hastened. Similarly, in **sycosis, furunculosis, indolent ulcers, whitlow,** etc., Heuss employs compresses consisting of 6 to 8 folds of gauze wet with 95 per cent. alcohol and covered with an impermeable dressing. Kaiser employed alcohol dressings in 93 cases of various **inflammatory affections**, and claimed very gratifying results; the distinctive feature of this method was that as a preliminary step, all fatty matter is removed from the involved area with benzine and alcohol (Bulkley).

Permanent applications of strong alcohol of great service in combating all **inflammatory conditions** in which there is a tendency toward suppuration. It causes a local dilatation of the blood-vessels, and thereby the

formation of alexins and consequent greater capacity for resisting the spread of infection. Thick layers of gauze are saturated with alcohol and then covered with some impervious material. The dressing is left in place for days at a time, resaturating it with alcohol once every twelve hours. Graeser (Münch. med. Woch., July 17, 1900).

Following combination recommended as a clean and effective substitute for the ordinary lead and laudanum dressing:—

℞ *Morphinæ acetatis*.. 0.65 Gm. (1 gr.).
Liq. plumbi subacetatis ..... 30 c.c. (1 oz.).
Alcoholis ...q. s. ad 120 c.c. (4 oz.).

M. Sig.: Apply on 1 layer of muslin or cotton and allow to evaporate. W. Brady (N. Y. Med. Jour., April 24, 1909).

The benefit derived from the use of the tincture of arnica in **sprains,** and spirit of camphor in **mastitis,** seems to depend entirely on the cooling produced by the rapid evaporation of the alcohol contained in these preparations. The benefit derived from the popular "alcohol rub" is entirely a matter of suggestion, and its supposed strengthening properties are mythical. Alcohol is not absorbed when rubbed on the skin. When used in this way in depressed conditions, it is liable to do harm, by reducing the body temperature when it should be sustained. Olive oil or cacao butter should be used instead of alcohol in massage. G. A. Graham (N. Y. Med. Jour., May 8, 1909).

Alcohol recommended as a final application in all cases of **wounds,** dressing with either plain or carbolized gauze. In **bruises** and **sprains** equal parts of extract of witchhazel and alcohol, applied as hot as can be borne, gives much better results than liniments or any of the clay and glycerin mixtures, and is much more agreeable to the patient. In **burns** and **scalds,** with suppuration, alcohol is an ideal application, and where carbolic acid is indicated it can be used in any strength if followed immediately with alcohol. This also applies to **suppuration** in all kinds of wounds. In patients confined to bed for any length of time, the use of alcohol after bathing **prevents bedsores.** Alcohol is one of the best antiseptics to clean instruments outside of an operating room. The hypodermic needle will always be ready if kept in alcohol, and there will be no need of inserting wires in it. It is best not to use a weaker solution than 60 per cent. of alcohol. Care is required, however, to get pure alcohol, as so many inferior brands are offered, which, if used, give disappointing results. S. S. Royster (Intern. Jour. of Surg., Oct., 1909).

Reports concerning the therapeutic uses of alcohol in dermatology have recently been reviewed by Bulkley. In **eczema** Unna recommends an alcohol dressing having the following composition: Sodium stearate, 6 parts; glycerin, 2.5; alcohol, to make 100. This has the advantage of greater permanency of effect than the rapidly evaporating pure alcohol, can be employed where the application of a bandage is impracticable, is non-irritating and strongly bactericidal. In **herpes simplex** as well as **herpes zoster,** the virtues of alcohol, applied on cotton and renewed at frequent intervals, were pointed out by Leloir and Dupas; if it be applied in the stage of erythema the eruption will disappear in a few hours; if in the vesicular stage, in the course of a few days. Leloir recommends that a small quantity of phenol be added, in order to alleviate further the burning and pain. In **lupus erythematosus,** striking results were obtained by Hebra, Jr., and by Kohn from the frequent application of alcohol,—40 to 50 times daily. Continued applications of alcohol led to cure in a case of **favus** reported by Cantoni. In **acne rosacea,** Abrahams has given subcutaneous injections of 20 to 30 drops of 95 per cent. alcohol,

repeated at most three times a week, and found that, after a temporary local anemia, the injections produced a hyperemia lasting for some hours, by which obliteration of the dilated vessels could be secured, providing the treatment be kept up for two or three months.

In **frost-bite, insect-bites,** and **itching** conditions in general the local anesthetic property of alcohol comes into play. According to Lauder Brunton, the itching in **pruritus ani** can be checked with absolute alcohol.

In **sprains** and **contusions** a rubefacient as well as a cooling effect is exerted.

In **fever** the body temperature may be lowered by bathing the surface with alcohol, diluted with 2 parts of water.

Applied to **aphthæ** or **sluggish ulcers** of various kinds, alcohol, undiluted, acts as a stimulant to the processes of repair.

Used hot in a 10 to 20 per cent. solution, alcohol has long been used as a gargle in **tonsillitis** and **pharyngitis.**

In the prophylaxis of **bed-sores** and of **cracked nipples,** dilute alcohol is very effective when systematically rubbed over the areas exposed, hardening the skin so that it is rendered more resistant to external influences, and bringing an increased amount of blood to it, thus antagonizing local necrosis. Where the nipples are already the seat of fissures or excoriations, alcohol will not only tend to relieve discomfort by obtunding the sensory nerve-endings, but will harden the surrounding healthy skin and, by coagulating the albumin in the secretions of the raw surfaces, cover these areas with a thin, protective film. The same astringent property of alcohol is of value in the treatment of **hyperidrosis** (excessive sweating) and **tender feet.**

As a hemostatic, alcohol is of some value in **minor hemorrhages,** especially where there is merely an **oozing** of blood from ruptured capillaries.

As a solvent of fatty substances, and likewise as a bactericidal agent, alcohol is of value when applied to the hands and operative area previous to minor surgical procedures. The removal of fatty material from the skin surface facilitates the action of germicides, such as mercury bichloride, subsequently applied. According to von Bruns, the value of alcohol in the **preparation of the skin before operations** is due not alone to its solvent and germicidal properties, but also to the fact that it hardens the skin and thereby keeps the deeply lodged bacteria from coming to its surface. That this factor in the action of alcohol is not in reality of great moment, however, would seem to be suggested by the recent experimental work of Ritchie, which tends to minimize the importance of the sweat-glands and hair-follicles of the normal skin as restive places for bacteria.

A dilution of alcohol of 55:100 is toxic to staphylococci, and is but slightly inferior to 1:1000 corrosive sublimate, and equal to carbolic acid in 3 parts per 100. Alcohol to which is added an alkali for the purpose of saponifying fat greatly increases the disinfecting powers. A dilution of 80 parts in 100 is an exceedingly efficient **disinfectant for the hands.** G. Fisher (La presse méd., July 7, 1900).

Property of alcohol in the **sterilization of the hands.** It is in abstracting air from the pores and fissures of the skin that the true value of the application lies; a previous treatment with alcohol enables subsequent aqueous solutions to penetrate much more thoroughly and completely into all the macroscopical and microscopical interstices

of the cutaneous surface. Braatz (Münch. med. Woch., July 17, 1900).

In the various preparations of alcohol, those with a higher specific weight have more energetic **disinfectant** action. The most energetic preparation is 40 per cent. alcohol, which boils at about 90° C. Frank (Münch. med. Woch., Jan. 22, 1901).

Advantages of **skin disinfection** with alcohol pointed out. If the skin is bathed and shaved, then rubbed for five minutes with sterile gauze saturated with absolute alcohol, its disinfection is accomplished more perfectly than by any other physical or chemical method. Dehydrated alcohol or wood alcohol may be used instead of pure grain alcohol in order to save expense. For effectiveness it is essential that the alcohol used be nearly or quite absolute alcohol. Meissner (Beiträge z. klin. Chir., S. 198, 1909).

Experiments with von Herff's method of **disinfecting the hands** with acetone alcohol. It is thought that the combination of acetone enables the mixture to be used on all portions of the body, and attacks the fatty tissue and disinfects it more thoroughly than alcohol alone. The use of the nailbrush may be omitted, and a longer disinfection is obtained by this method. The use of soda solution for ten minutes increases the efficiency of the method somewhat. As the method is a simple one, it is especially adapted for the use of nurses and midwives. In the clinic the alcohol employed was 95 per cent., and the proportion of acetone, after some experiment, was fixed at 10 per cent. The most efficient combination, however, seemed to be that of 50 per cent. alcohol and 50 per cent. acetone. Preliminary cleansing with soap, water, and brush was omitted. Four minutes were occupied in disinfection. The method did not seem to irritate the skin, and one of the staff, who acquired eczema through other methods of disinfectjon, was much improved. Oeri (Zeit. f. Geb. u. Gyn., Bd. lxiii, Hft. 3, 1908).

Alcohol used as a **disinfectant** found effect for a short time only—for operations not exceeding five minutes in length. Pfisterer (Zeit. f. Geb. u. Gyn., Bd. lxiii, Hft. 3, 1908).

Comparative study made of the value of alcohol and of Grossich's iodine method. The two methods appeared equally good, though the iodine method is more rapid. In the alcohol method the hands are washed with soap and water, dried with a towel, then scrubbed for five minutes by the clock, with gauze wet in 95 per cent. alcohol; finally the hands are dried. No gloves are worn. During the operation the hands are dipped in alcohol, without trying to get rid of the blood on the hands, which are blood-stained at the end of the operation. For the field of operation the author uses alcohol or tincture of iodine on the dry skin. There is no previous preparation, with the exception of a bath the night before. Grekow (Arch. f. klin. Chir., S. 1073, 1909).

Two years' experience has demonstrated to the author's satisfaction the superiority of this simple and convenient method over all other techniques in which soap and water are permitted. He rubs the field of operation for five minutes with the 10 per cent. alcohol acetone solution and then applies a varnish, the formula for which is 10 parts each of benzoin and dammar resin in 100 parts ether, stained with 20 per cent. of an alcohol iodoiodide solution (7 parts iodine, 5 parts potassium iodide and 100 parts alcohol). Von Herff (Therap. der Gegenwart, Dec., 1909).

Comparative tests of various methods of **sterilization** performed. A 5 per cent. alcohol solution of tannin surpasses all the other techniques with the exception of tincture of iodine; it ranks with this, while it is free from its disadvantages. The tannin solution is applied to the hands for two minutes and to the field of operation for one minute; the previous use of water does not affect it. Zabludowski (Deut. med. Woch., March 2, 1911).

Finally, the value of alcohol as a preventive and curative agent in **carbolic**

acid burns is well recognized. The phenol is dissolved by the alcohol.

Efficiency of alcohol as an antidote to carbolic acid questioned. According to experiments high concentrations of alcohol and low concentrations of carbolic acid seemed to increase the toxicity of the latter. A 1:100,000 solution of carbolic acid was more toxic in the presence of 10-per-cent. alcohol than without it. The antagonism of alcohol to carbolic acid observed in practice probably depends on a physical rather than a chemical basis. Taylor (Jour. of Biol. Chem., Dec., 1908).

The peculiar phenomena by reason of which alcohol has been acclaimed an **antidote to phenol** are the result of its solvent and repellent properties and not of any chemical antagonism. Phenol, though a powerful corrosive, limits its destructive progress by the formation of an albuminous coagulum. Alcohol is of great value externally when used early, but when used late the destruction of tissue is not prevented, although the appearance is better. On account of the repellent and solvent properties of alcohol it is dangerous to leave it in the stomach together with the phenol. The treatment advised is, first, lavage with some solution, as the magnesium-sulphate, albumin mixture, followed by lavage with a solution of alcohol as a clearing agent. Novack (Mo. Cyclo. and Med. Bull., Aug., 1909).

Internally, there are but five indications for alcohol that justify its use under our present knowledge: (1) As an **antidote to carbolic acid**—only when it can be administered shortly—within one or one and a half hours—following the poison. Life saved in two instances by this measure. Diluted alcohol (50 per cent.) is better than brandy and whisky. (2) As a fuel, in **fevers**, exhausted states of the body, and **marasmus** of infants. Here our purpose must be to give only a quantity that the patient can metabolize or oxidize and derive therefrom energy. When we can detect alcohol on the breath, the dose must be decreased. An average dose of alcohol for this purpose is 2 to 4 c.c. (4 to 8 c.c. whisky; 30 c.c. or less of wine, according to variety; 10 to 30 c.c. of any of the "medicinal" proprietary foods), given every four to six hours, with or following other food, preferably. (3) For the **chill of febrile stages**—such as **pneumonia, malaria, septicemia**—here alcohol in medicinal dose (*e.g.*, 15 c.c. or more of whisky) opens the surface capillaries that are contracted in chill and so gives a sense of warmth to the patient, lowers the fever, and through cerebral depression blunts the patient's mental anguish. Of course, the chill of hemorrhage, shock, or other condition not accompanied with fever contraindicates alcohol. (4) To reduce **fever.** In some cases of **typhoid,** where the plunge or sponge bath fails to lower an excessive temperature, 30 c.c. of brandy immediately preceding the bath will insure a notable reduction, by driving the warm blood to the surface to be returned cooled to the internal organs. In the presence of a low arterial tension or a very weak heart muscle, however, this use of alcohol would hardly be justified. (5) As a **narcotic,** in many persons of advanced years and a few with earlier arteriosclerosis who are apt to suffer from **insomnia,** a "night-cap" of brandy in the form of a "sling" will act favorably and is free from the unpleasant symptoms that often follow the use of the old or new hypnotics. Fear of habit, in this instance, need hardly be considered. Prescribing alcohol to enable a patient to withstand the strain of having a tooth extracted, an abscess opened, or wound sutured, on the other hand, is crude therapeutics. William Brady (N. Y. Med. Jour., April 24, 1909).

Alcohol Injections.—Neuralgia and Neuritis.—Injections of alcohol into or in the vicinity of nerve trunks for the purpose of relieving pain are employed particularly in **trifacial neuralgia** (tic douloureux) and in **sciatica,**

but have also been utilized in intractable neuralgias of other nerves, in neuritis following influenza, in blepharospasm, and recently in laryngeal tuberculosis.

The Schlösser plan of injection in tic douloureux, viz., the injection of alcohol into the second or third divisions of the trifacial nerve at their emergence from the cranium, has been extensively tested and, owing to the prompt benefit it affords, is growing in favor, though it cannot be considered as a uniformly curative measure, a certain number of cases relapsing after a variable number of months of freedom from pain. The mode of action of the alcohol in these cases was elucidated in 1910 by Schlösser, who found through animal experimentation that alcohol of 70 to 80 per cent. concentration, when brought in relation with a nerve, caused degenerative processes to take place in all the elements of the nerve except the neurilemma. Leszynsky, reporting 15 cases of tic douloureux successfully treated by alcohol injection, stated his belief that this method is practically equivalent to a section of the nerve, with the added advantage of absence of an operative scar. The method is not applicable, however, to neuralgia of the first division of the trifacial, a certain amount of danger having been found to attend injections of this branch.

Report of 63 cases, 41 women and 22 men, in which alcohol injections were given. In 21 cases the second divisions were involved, in 31 cases the first and second divisions, and in 11 cases the second division alone. As regards results, the cases were divided into two classes: (1) those previously treated surgically; (2) those not so treated. The cases of the first class were not half as much benefited by alcohol injection as those of the second. In 1 case, previously operated upon at three different times, no effect on the pain was produced until the branches of the trigeminal on the sound side had been injected. With the exception of 2 cases the results were uniformly good. Three of the cases had already remained well from eighteen months to two years. In most cases the treatment must be resumed at the end of six months, but recurrences are apt to be less severe each time they appear. Sicard (Presse méd., May 6, 1908).

Report of 190 cases of trifacial neuralgia injected with alcohol since 1906. The number of injections varied from 2 to 10, the average being 3. Results: 5 failures and 185 cases free from pain for varying periods. Kiliani (Med. Record, June 5, 1909).

Alcohol injections given in 75 cases of unmistakable tic douloureux, invariably with relief. Thirty-six patients were between 60 and 70 years of age, 13 between 70 and 80 years, and 1 over 80 years. All the patients had already tried other forms of treatment and a considerable number had undergone operation. Alcohol of 85 per cent. strength was used, 4 grains of cocaine to the ounce being added. About 2 c.c. of the solution were injected each time. The injections were made with a straight needle about 10 cm. long, 1.5 mm. thick, and fitted with a stylet or obturator, the blunt end of which was flush with the needle-point. The sharp point was used to puncture the skin, after which the stylet was pushed home, making a blunt instrument for the remainder of the penetration. The needle is introduced at the lower border of the zygoma, the aim being to attain the inferior maxillary division of the nerve at the emergence from the foramen ovale (about 4 cm. in depth), and the superior as it leaves the foramen rotundum. Patrick (Jour. Amer. Med. Assoc., Dec. 11, 1909).

Laryngeal Tuberculosis.—Alcohol injections into the superior laryngeal nerve for the relief of dysphagia in tuberculosis of the larynx were introduced by Hoffman, of Munich. Recent

experiences with this procedure have only served to confirm and establish its usefulness as a palliative measure.

> Alcohol injections into superior laryngeal nerve employed in a series of cases with gratifying results. The duration of the relief experienced is the striking feature of this method of treatment. The solution employed consists of 2 grains of hydrochloride of beta-eucaine in an ounce of 80-per-cent. alcohol. The patient being placed horizontally, the sound side of the larynx is pressed toward the middle line with the thumb of the left hand so that the affected half projects distinctly; the other fingers of the hand lie on this half. The index finger enters the space between the thyroid cartilage and the hyoid bone from without until the patient announces that a painful spot has been reached. The nail of the index finger is now placed upon the skin in such a way that the point of entrance for the needle lies oposite its middle. The needle is pushed in for about 1.5 cm.; this distance is marked off on the needle perpendicularly to the surface of the body. According to the thinness of the subcutaneous layer of fat, the perforation has to be more or less deep. The needle is then carefully moved so as to seek a spot at which the patient feels pain in the ear. The syringe, filled with the alcohol, warmed to a temperature of 45° C. (113° F.), is screwed to the needle and the piston slowly pressed down. The patient now feels pain in the ear, the passing off of which he indicates by raising his hand. During the operation swallowing and speaking must be avoided. The injection is kept up until no further pain occurs in the ear. Then the needle is removed and collodion applied. The point of the needle is bevelled much more obtusely than the ordinary hypodermic needle, to avoid the danger of puncturing a vessel. Dundas Grant (Lancet, June 25, 1910).

Tumors.—Carcinoma of the uterus was treated with alcohol as long ago as 1878 by Hasse, who made injections into the circumference of the tumors in 3 cases with good results; after twenty-three years the patients were alive and well. Obliteration of the blood-vessels and shrinkage of the tumor were found to have taken place, through connective-tissue proliferation around the growth. A similar plan of treatment has also been utilized in **cancer of the breast.**

As a palliative measure, interstitial injections of alcohol were used by Vulliet, of Geneva, in inoperable cases of **uterine cancer.** The benefit obtained was ascribed by him to the local ischemia induced.

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Philadelphia.

ALCOHOLIC NEURITIS. See Neuritis.

ALCOHOLISM, OR ALCOHOL INEBRIETY. —DEFINITION.— Alcoholism is frequently defined as the result, in the organism, of excessive consumption of alcohol. The term, thus interpreted, should refer only to individuals profoundly poisoned and diseased from this specific cause. Modern research has shown, however, that there exists a large class of cases in which the excessive use of alcohol is a predominant feature, but which are not accurately described by the term "alcoholism," viz., those in which the use of spirits is only symptomatic of a neurosis of different nature and causation. It is probable that at least 50 per cent. of all so-called alcoholics have suffered from disease of the nervous system before acquiring the alcoholic habit.

Inebriety, meaning a poisoned or stuporous state directly or indirectly the result of alcohol, is, in reality, **a**

more general term than "alcoholism," since it refers to the condition of all those who use alcohol to excess. This term is also employed, however, to designate toxic states resulting from the use of various other drugs, such as opium, cocaine, chloral, chloroform, etc.

[Alcoholism received very little attention as a distinct malady until recent times. Yet, there is abundant evidence that the excessive use of wine and beer was recognized as a disease in the civilization of Egypt at least seven or eight thousand years ago. This belief existed also in early Grecian times, and some very acute reasonings as to the causes and means of prevention were brought forth, although wine was, nevertheless, defined as a means of inducing a supposed highly esthetic condition of the mind. In later years, when alcoholism became widespread, and was given place among the great national vices, many physicians began to consider it as a disease and a curable one, and laws were passed based on the recognition of this fact.

Although the physical nature of inebriety had been recognized in many directions and fragmentary statements concerning it had appeared in foreign literature, it was reserved for Dr. Benjamin Rush, of Philadelphia, to give it a permanent setting in a small book published in 1809. He urged that alcoholism was a disease curable and preventable. The medical interests of the subject seem to have dated from this point. Although many foreign authors have given very minute descriptions of the pathological effects of alcohol on the body, the disease of inebriety or alcoholism has been given but little attention. To American physicians, therefore, is very largely due the promotion of this idea.

The creation of an institution at Binghamton, New York, in 1864, for the treatment of inebriety as a disease brought the subject into prominence, and gave permanence to the belief which had persisted in the midst of more or less uncertainty through all the centuries past. The organization of a society for the study of the subject, and the publication of a journal as its organ, still further developed, and brought into public notice, this great question. Though sharply condemned at first, and pronounced an extreme and untenable view, it has grown to be a settled fact, accepted in practically all centers of scientific inquiry, that the inebriate and alcoholic is suffering from a distinct neurosis—a disease requiring special study and treatment.

During the last half-century a considerable literature on this subject has appeared, much of it merely formative and dogmatic, but clearing the way and establishing fundamental principles for a more rational view and explanation of the morbid processes entailed.

The amount of alcohol consumed per capita has been increasing, and it is fair to judge that this indicates an increased number of persons to be suffering from the disease produced by it. Researches into the etiology of various maladies show that as a source of degeneration and as a contributing cause the use of alcohol is a very prominent factor.

Whether there are more alcoholics than formerly, meaning by this persons who are notoriously affected by the use of spirits, is an open question. Many are convinced that the number of inebriates or alcoholics is diminishing, and this would appear to be true from a mere casual observation. Fewer men are arrested for drunkenness on the streets, while the number of persons who are in the incurable stages apparent to all is diminishing.

It is, nevertheless, evident that the mortality among persons who drink alcohol has greatly increased, and that it is not possible in this country to drink alcohol in so-called moderation, according to the European standards. This is illustrated by the frequency and extreme fatality of pneumonia in alcoholics. Cerebral hemorrhage is another common sequela, and is given as the cause of death in a large proportion of cases with an alcoholic history. Nephritis and cirrhosis are other familiar causes of death in persons addicted to alcohol. The mortality in all these diseases being high, it is evident that alcohol is a dangerous beverage and drug.

The high degree of mental activity and nervous strain characteristic of American civilization has much to do with intensifying the toxic action of alcohol and lowering the resisting power and vitality. The average

American business man, too, is far more susceptible to the poisonous effects of alcohol than individuals of the same class in Europe.

On the whole, alcoholism in America is a far more serious and fatal disease than in any other country. The results from the use of spirits are more destructive, and the injury less easily repaired. Alcohol is a more grateful and fascinating narcotic in America than elsewhere, because it produces seductive effects of relief, and covers up exhaustion. The enormous sale of proprietary drugs containing alcohol is evidence of this. Even in colleges and training schools many young men are impressed with the accuracy of the old-time theory that alcohol has a stimulant and invigorating action, and use it upon the advice of their teachers or from the contagion of their associates.

On the whole, the fact is becoming more and more prominent not that alcoholism is of greater prevalence, and the victims more numerous, but that any use of alcohol is dangerous to both brain and muscle workers, and is obstructive to all success and progress in every department of life. T. D. Crothers.]

> Alcohol really plays an enormous rôle in bringing about degeneration of the race. This is most clearly seen in the growing inability of mothers to nurse their offspring; thus, when mother and daughter of one family were not obliged to resort to artificial feeding, the father was a drunkard in only 2.6 per cent., while, where both were unable to nurse, a history of excessive drinking was obtained in 42.2 per cent. All cases of functional derangement owing to imperfect condition of the nipples were ruled out. The condition is hereditary, for if the mother has lost the power it will never be regained in that particular generation.
>
> Other stigmata go hand in hand with deficient nursing capacity, and a pronounced disposition toward tuberculosis, nervous diseases, and psychoses is very evident. The offspring of alcoholics also suffer more frequently from carious teeth. G. v. Bunge (Virchow's Archiv, Bd. clxxv, Nu. 2, 1904).

TOXICITY OF THE ALCOHOLS.—All alcohols are poisonous, though their toxic power varies considerably in accordance with the variety of alcohol ingested. Thus, the heavier members of the series (propyl, butyl, and amyl alcohols), which have a higher boiling point than ordinary ethyl alcohol, are more toxic than the latter. Methyl alcohol, though the lightest of all the alcohols, is, nevertheless, more poisonous than ethyl, forming an exception to the general rule that the toxicity of the alcohols rises with the increase in their molecular weights. The toxic action of methyl alcohol, or "wood spirits," has already been described (*v.* Methyl Alcohol). That of ethyl alcohol, which forms the subject of this article, is modified, to a certain extent, by the nature of the preparation containing it. Spirits exert a more rapid toxic effect than wines or beers, owing to the greater concentration and quantity of alcohol present in the former. The different kinds of spirits themselves exhibit differences in toxicity in accordance with the material from which they are produced, the variations being due to differences in the amount of certain additional toxic compounds contained, such as aldehyde, ketones, furfurol, ethers, etc. Thus, according to Dujardin-Beaumetz and Audigé, spirits made from wine (brandy) are the least toxic; next follow in order spirits made from perry, cider, grain, beets, and molasses; finally come spirits made from potatoes and sorghum, which are the most toxic, owing to the relatively large proportions of isobutylic and amylic alcohols they contain. Spirits of inferior grade are especially dangerous because they are made with impure

alcohol, the disagreeable taste and odor of the impurities being masked by admixture of artificial flavors and essences (Pouchet). In addition to the true spirituous liquors already referred to, there is a large group of liquors representing a solution of various aromatic principles, either of vegetable origin or produced synthetically, in a menstruum of alcohol. Here the effects of the aromatic principles are added to those of alcohol, and these fluids may, therefore, be divided into two groups, according as the tendency of the aromatic principle contained is to produce epileptiform convulsions (best illustrated in the case of absinthe), or to bring on stupor (anise, mint, angelica, etc.).

The fatal dose of alcohol varies within wide limits. The factors influencing it include not only the individual's habits with respect to alcoholic indulgence, but in addition his state of health, the climate and temperature, and the rapidity of absorption (Pouchet). The average lethal dose has been stated to be 60 to 180 Gm. (2 to 6 ounces, approximately). Less than 1 pint of whisky has sufficed to cause the death of an adult. In the lower animals, Lussana and Albertoni give 6 Gm. (1½ drams) per kg. of body weight as the minimum lethal dose.

VARIETIES.—There are two forms of alcoholism: (1) the *acute,* in which alcoholic poisoning is speedily manifested in active excitement and disturbance, or in which a sudden exacerbation of the disorders attending the chronic type gives rise to a correspondingly marked symptomatic activity; (2) the *chronic,* in which the continued ingestion of alcoholic beverages in more or less considerable amounts sets up gradually progressing pathological changes in the various organs and tissues, thereby giving rise to chronic disorders of each of the parts thus affected.

Under acute alcoholism are to be considered not only acute alcoholic poisoning, intoxication, or "drunkenness," but also acute alcoholic epilepsy, acute alcoholic hysteria, acute alcoholic delirium or delirium tremens, and acute alcoholic mania or mania a potu.

ACUTE ALCOHOLISM.

DEFINITION.—A condition resulting from the ingestion, within a short period, of alcohol in sufficient quantity to produce exaggerated physiological effects or actual poisonous effects. The amount required to intoxicate varies widely according to the natural susceptibility of the individual, and to whether or not his organism has become accustomed to the action of alcohol through repeated use.

SYMPTOMS.—Three stages are discernible in this condition: The first is that of beginning vascular relaxation and primary excitation. The intoxicated individual is usually lively, merry, agile, and joyous; all excitement and energy; in the highest spirits, cheerful, hopeful, and communicative; mercurial and confiding, often telling of his private affairs to strangers. There is a warm glow on his countenance, and he appears at his best. Gradually his spirits rise still higher; he becomes more demonstrative in love or in argument, more emphatic in his gestures, more furious in his fun, and very much louder in his laughter as the second stage is ushered in. With this he becomes much less reasonable and amenable, incoherence of thought and speech gradually sets in, the imagination rev-

els, exaggeration is a prominent feature, and the emotions dominate the subject, intellect, reason, will, and conscience rapidly fading into the background. In some cases his thoughts, speech, and actions are exaggerated. In other instances they are transformed, the habitually modest, retiring man becoming a boaster and a braggart, the truthful a liar, the meek violent. With all this, the speech thickens, the lower and then the upper limbs cease to act in unison; the intoxicated cannot stand, but staggers with a paralytic unsteadiness, the muscles becoming flabby and feeble. The third stage, that of "dead drunkenness," reveals the subject unconscious, with the pallor of apparent death on the face, extreme coldness of the skin, accompanied by total insensibility, and an utter disregard of the "world without." Sensation, perception, volition, and emotion, all are absent. Through this living death there lingers in the heart the only spark of vitality that keeps the unconscious drunkard alive, till the faculties have emerged—if, indeed, they do emerge—from the depth of narcotism into which they were plunged. The first, pleasurable stage, and the second stage, less pleasant, may vary in intensity and duration, but the third stage, that of insensibility, usually lasts from six to twelve hours (Norman Kerr).

In the first stage, that of exhilaration or apparent stimulation, there is an increase of the heart-rate, and frequently a rise in the blood-pressure. The breathing is generally hastened and becomes deeper. The skin is reddened, and the surface temperature rises slightly, owing to the paralyzing effect of the alcohol on the superficial blood-vessels, through which an increased amount of warm blood, therefore, courses. The pupils are of normal size or slightly dilated, and the higher psychic processes—those involving continued attention, reflection, judgment, self-control—gradually fall in abeyance.

The manifestations of the second stage are similar to those of the first, but more pronounced and with the added presence of motor inco-ordination, due to the effects of the drug on the cerebellar and spinal centers. A subjective feeling of intense peripheral warmth is experienced, the pulse is full and bounding, and the respiration hurried and frequently irregular. Incoherence of speech and staggering gait are the most prominent symptoms of this stage, though the relative time required for the appearance of each varies notably in different individuals, some getting drunk first "in the legs," others "in the tongue." Nausea and vomiting may also appear, and toward the close of the period facial pallor and a tendency to syncope may be present.

In some instances the first and second stages, instead of showing the individual in a condition of general excitement, are characterized by depression of spirits, merging more or less insensibly into the ultimate stage of total cerebral inaction. In another group of cases, on the other hand, the initial excitement is unusually pronounced, the subject crying out loudly, experiencing illusions, and even committing acts of violence.

The third stage of alcoholic intoxication, that of unconsciousness and deepening coma, is characterized by successive abolition of the functions of various portions of the central nervous system. The spinal cord and cranial nerve-centers becoming depressed, motion and sensation are progressively lost. The subject cannot be awakened

by shouting in the ear; his musculature, including the sphincters, is completely relaxed, and general sensibility is abolished. The pulse may be full and approximately normal in rate, or may be feeble and slow. The breathing is slow, labored, and sometimes irregular —an indication of beginning paralysis of the medullary centers. It is also stertorous, owing to relaxation of the muscles of the soft palate. The skin is now pale and covered with cold sweat, though the face is bloated, the lips purplish and swollen, and the conjunctivæ markedly congested. The temperature of the body is lowered, the rectal reading being invariably reduced by 1, 2, or even 4° F. (Butler). The pupils may be dilated, especially in cases of severe intoxication, and the light-reflex abolished. The knee-jerks and other reflexes are likewise lost.

In cases terminating fatally, death takes place from respiratory arrest after a period ranging from one-half hour to fifteen or twenty hours (Pouchet).

When an unusually large amount of alcohol has been taken—true cases of acute alcohol poisoning, as distinguished from those of ordinary "intoxication"—the stages of excitement are apt to be of very brief duration (especially if the alcohol has been taken on an empty stomach), the subject sinking promptly into coma. Vomiting, swallowing movements, piercing cries, and muscular contractures betoken a brief primary excitation of the nerve-centers, after which depression quickly appears, indicated by respiratory and circulatory disturbances and general anesthesia. Convulsions and death from respiratory paralysis or edema of the lungs may finally result.

Acute alcoholic intoxication in some instances brings forth phenomena foreign to the conventional manifestations already described. Thus, in some cases, an *epileptic attack* is the most prominent result. It may occur either in an individual already subject to epilepsy, in which event the alcohol acts indirectly, being merely an exciting cause of the paroxysm; or, it may take place as a direct result of the effects of alcohol, in persons previously not subject to epileptic seizures, under which circumstances the condition may be termed a true *acute alcoholic epilepsy*. Again, an outburst of *acute mania* may be the result of alcoholic intoxication. Such a result is seen most frequently in cases of incipient or fully developed general paralysis. Similarly imbeciles and epileptics are particularly likely to experience hallucinations under the influence of alcohol, and to commit acts of violence upon the impulse of the moment (Pouchet). Finally, *hysterical paroxysms* may also result from the consumption of alcohol, even in relatively small amounts, and in individuals otherwise never hysterical (Kerr).

DIFFERENTIAL DIAGNOSIS.—In the first two stages of acute alcoholic intoxication, those of excitation and of motor inco-ordination, the symptoms present are sometimes distinguishable with difficulty from those produced by the ingestion of other drug excitants, such as opium, or from those of apoplexy, unless, as is frequently the case, a clue to the cause of the disturbance is furnished by the finding of alcohol on the premises, or a history of alcoholic indulgence can be obtained. In the case of apoplexy, however, the uncertainty is not likely to be of long duration, the symptoms of excitation soon passing off entirely, or being promptly replaced by coma.

A more important and difficult distinction is that to be made between the third stage of intoxication by alcohol, that of sleep and insensibility, and comatose conditions, such as uremia, apoplexy, concussion of the brain (in cases of fractured skull), acute opium or chloral poisoning, and diabetic coma. In police stations so-called "drunks" are often not such, and a fatal result may thus be practically insured. An alcoholic odor of the breath is, of course, characteristic of alcoholic intoxication, but it is not pathognomonic; an individual unconscious from another cause may, perhaps, have taken or been given alcohol in quantity insufficient to intoxicate.

Though, according to quite a number of observers, pressure on the supraorbital nerves in their respective notches will elicit signs of life in the alcoholic when it would not in other states of unconsciousness, the fact remains that mistakes have been, and are still, frequently made in the differential diagnosis between ordinary cases of "drunkenness" and cases of fractured skull. It may, indeed, in some instances be practically impossible, even for the medical expert, to form a correct opinion as to the causative agent until time has been given for the disappearance of the alcoholic symptoms.

To facilitate the recognition of the morbid condition that may be present, the following chart is presented.

PATHOLOGY.—The most prominent of the post-mortem appearances in fatal cases of acute alcoholic poisoning is cerebral congestion. While no noteworthy destructive lesions of the cerebral substance proper may be found, hemorrhagic extravasations may quite frequently be discovered in the meninges at the base of the cerebellum, in the subarachnoid space, or even in the lateral ventricles (Pouchet).

Marked congestion of the lungs and respiratory passages is also commonly a feature. The right heart cavities may be found distended with semifluid blood. Tardieu in one case discovered apoplectic extravasations of blood in the lungs. The gastrointestinal mucous membranes may also be markedly congested, though such a condition is, of course, in no sense peculiar to alcohol poisoning. In the case cited by Kerr, of a man found dead after a drinking bout, "the mucous membrane of the stomach was so inflamed and angry, with patches of a deeper hue extending over the pyloric surface to the duodenum, and a grumous, slightly mucopurulent exudation from bleeding points, that arsenical poisoning was suspected." Hepatic congestion we would naturally expect to, and frequently do, find as a post-mortem evidence of acute alcohol poisoning.

Dana studied the brain-cells in 10 cases of acute alcoholism by the Nissl method of staining with methyl violet: (*a*) patients who died of alcoholism with all the symptoms of meningitis showed congestion of the membranes (pia, arachnoid), with some edema in their texture; (*b*) microscopic examination rarely showed any migration of leucocytes or anything approaching encephalitis; (*c*) the larger (pyramidal and giant) nerve-cells showed pigmentation to an intense degree, the pigment being diffused through the cell-body; (*d*) the cytoplasm showed various degrees of degeneration (fatty and granular); (*e*) the cell-body generally was shrunken, and the nucleus partially so; (*f*) pericellular nuclei had prolif-

DIFFERENTIAL DIAGNOSIS OF ACUTE ALCOHOLISM.

	ACUTE ALCOHOLISM.	UREMIC COMA.	APOPLEXY.	CONCUSSION OF THE BRAIN.	OPIUM POISONING.	DIABETIC COMA.
Consciousness.	Not absolutely lost; can usually be aroused by shouting or shaking.	Completely lost.	Partially or entirely lost.	Rarely completely lost.	Profound stupor.	Completely lost.
Temperature.	Often subnormal.	Variable; not uncommonly subnormal.	Usually rises above normal.	Subnormal.	Often subnormal.	Subnormal.
Pulse.	Frequent; later weak.		Slow, full, tense.	Frequent and weak.	Slow, full.	Frequent.
Respiration.	Stertorous.	Often Cheyne-Stokes.	Slow, stertorous, and puffing.	Slow and shallow.	Very slow.	Long-drawn inspiration, sighing expiration.
Pupils.	Usually dilated; equal, and react to light.	Normal or dilated.	Dilated or contracted; sometimes unequal.	Usually dilated; equal, and react to light.	Contracted.	Dilated.
Skin.	Face flushed.	Waxy pallor.	Face flushed or cyanotic; sometimes pale.	Cold and pale.	Face flushed, sometimes cyanosed.	Sometimes cyanosis.
Reflexes.	Sluggish or abolished.		Lost on paralyzed side and often on sound side.	Sluggish or lost.		Lost.
Convulsions.	Uncommon, except in dangerous cases.	Common.	Usually only at time of stroke.	Late, if any.	Uncommon.	Rare.
Paralyses.	None.	Rare.	Hemiplegia.	Transient, if any.	None.	None.
Odor.	Alcoholic odor of breath.	Urinous odor sometimes.	None.	None.	Laudanum odor on breath sometimes noticeable.	Sweet odor of breath.
Urine.	Contains alcohol; otherwise not characteristic.	Contains albumin, casts, and decreased urea.	Not characteristic.	Not characteristic.	Not characteristic.	Glycosuria, acetonuria, diaceturia.
Emunctories.	Frequently incontinence of urine and feces.	Anuria common.		Retention of urine; incontinence of feces.	No involuntary evacuations.	
Special signs.		Edema of face and feet; albuminuric retinitis.	Deviation of head and eyes to side opposite that of paralysis.	Probably evidence of trauma to head.		

erated, and were freely present in the pericellular sacs. In cases where death was due to exhaustion the shrinkage of cells was marked.

TREATMENT.—In common drunkenness, where the pallor and depression are not too marked, and where the respiration is active and the pulse is good, the patient may be allowed to sleep. The elimination of the poison occurring rapidly, he awakes after several hours with more or less headache, depression, irritability of the stomach, and tremor as results of the intoxication. **Light and easily digested food, Vichy** and **milk** as beverages, and a light **aperient**, if required, will soon be followed by recovery. **Ammonium carbonate, 1** dram (4 Gm.) in a glassful of water, will counteract depression. Alcohol for the latter purpose should never be given.

In severe cases in which there is

a tendency to coma, with shallow breathing and feeble pulse, the probability that a quantity of alcohol is still present in the stomach should be borne in mind. The stomach should be emptied by means of the **stomach tube** and washed out with warm water. **External heat** should be applied, especially to the abdomen and feet, and the patient placed in a warm room. Depressing emetics are contraindicated, since the depression is already excessive and the dangerous feature. No alcohol should be administered as a stimulant. Hypodermic injections of **strychnine, atropine,** or **digitalis** are of great value to restore the equilibrium of the circulation.

In acute alcoholism attended by excitement and perhaps convulsions, especially in robust patients, free emesis should be procured promptly by giving 1/10 grain (0.006 Gm.) of **apomorphine hydrochloride.** This usually causes vomiting in four or five minutes, and is then followed by relaxation and sleep. **Digitalis** or **digitalin** has also been recommended in this class of cases to counteract the morbid effects of the poison on the heart and circulation, and thus restore the patient to his normal condition much sooner. Hot (105° F.) rectal enemata of **saline solution** are also valuable in these cases during the acute attack to reduce the toxicity of the blood, if the enema is retained long enough to insure absorption. **Hypodermoclysis** should be resorted to if the rectal injections do not prove satisfactory.

> To obtain the hypnotic action of **apomorphine hydrochloride** it should be given hypodermically. The dose cannot be fixed. It is well to begin with 1/30 grain, or less, and to repeat this or give a slightly larger dose within a short time. Should vomiting occur, the drug should be discontinued for several hours. Doses repeated in two or three hours have but little beneficial effect. The administration of apomorphine should not be repeated in patients who are weak. The hypnotic action of the drug lasts only a few hours, and when the patient awakes the condition is practically unchanged. The best results are obtain from the drug when it is followed in two or three hours by some recognized hypnotic. Apomorphine should always be given in fresh solution. W. Coleman and J. M. Polk (Amer. Med., March 8, 1902).

In the acute stage of alcoholism, a very useful drug for hypodermic injection is **apomorphine.** In the excitement of delirium tremens a small injection of this drug will at once produce a calm, the patient will yawn, and is fast asleep almost before he can be got to bed. This sleep is sometimes preceded by vomiting. As the patient is liable to faint if sitting up, the injection should be given when he is in a recumbent position. Usually about four hours' sleep is thus obtained. But apomorphine is no remedy for alcoholic craving; while a good way of commencing treatment, it is only temporary. The drugs to be relied on to do away with the craving for alcohol are **strychnine** and **atropine;** they should be kept in solution and the injections given into the biceps muscle twice or three times a day. Bolton (Brit. Med. Jour., Oct. 12, 1907).

The value of **apomorphine hydrochloride** in acute alcoholism was pointed out by C. J. Douglas, of Boston, in 1899, but remains almost unknown. The drug acts promptly when administered as an emetic in doses of 1/10 or 1/8 grain, and it acts with almost equal promptness when administered as an hypnotic. The alcoholic, however wild or noisy, will, as a rule, be peacefully sleeping in ten or twelve minutes after 1/20 to 1/30 grain is administered subcutaneously. This sleep may last several hours, when the patient awakens refreshed

and sober. Douglas employed the remedy, with these doses, in over 200 cases, mostly alcoholics, including cases of delirium tremens, and with gratifying results. Drs. Coleman and Polk, of Bellevue Hospital, New York, used it in over 300 cases of alcoholism; also with gratifying results. Dr. Rosenwasser, inebriatist to Newark Dispensary, Newark, N. J., has also used apomorphine in the same manner, and for the same purpose, and with equally satisfactory results. The dose administered was from 1/30 to 1/20 grain. With these doses, the hypnotic effect is secured in 67 per cent. of the cases. Even 1/40 grain, in the author's experience, is effective with some patients. A. M. Rosebrugh (Can. Jour. Med. and Surg., Oct., 1908).

Apomorphine is of great value in acute alcoholism. The desire for liquor in these cases becomes imperatively dominant. Apomorphine enforces sleep, and when the patient awakens his chain of thought has been broken and the attack is over in many cases. In all such cases the action of an emetic is of some value in sobering the patient and diminishing or abolishing the desire for more drink, and, therefore, the dose usually given is 1/10 grain by hypodermic injection, adding 1/30 grain **strychnine** if the heart is acting poorly. Whenever possible when given the injection the patient should be lying in bed, and basins should be in readiness, as the action of the drug is rapid. The author has always been able to secure the hypnotic effect. In many cases 1/30 grain given hypodermically will be found sufficient to induce sleep. If the general condition of the patient is fair the dose may safely be repeated in about three hours, if necessary, as the drug is not cumulative in its action. C. A. Rosenwasser (Med. Times, Dec., 1910).

CHRONIC ALCOHOLISM.

DEFINITION.—A condition resulting from the long-continued use of alcohol in excessive amounts. As was stated to be the case with acute alcoholism, the quantity of alcohol necessary to cause harmful results varies considerably in different persons. The manifestations of chronic alcoholism are varied. Many symptoms due to toxemia and functional derangements closely simulating organic changes are observed in the beginning. Later evidences appear of true organic disease, affecting one or more organs or systems of organs in individual cases. Thus the stomach, the nervous system, the circulatory organs, the kidneys, the liver, are all common seats of special invasion. In many cases the symptoms are very complex, and are not such as lead to the discovery of any particular organic lesion. As already stated, the alcoholism is itself sometimes secondary to a neurosis of other nature, in which event complexity of symptoms is to be expected.

Dipsomania signifies a condition, hereditary in origin, in which uncontrollable desire for alcohol is present at intervals only, the patient being free of alcoholic tendencies in the intervening periods.

Delirium tremens is another special manifestation arising from the prolonged effects of alcohol on the brain. It will be discussed later in a separate section of this article.

SYMPTOMS.—Most cases will exhibit in the beginning deranged digestion, fermentation in the stomach and bowels, constipation or diarrhea, muffled heart-sounds, irregular action with high-tension pulse, and increased dullness over the liver, perhaps with tenderness in spots. There is very commonly trembling, the hands are unsteady in their movements, the reflexes are diminished or absent, and there are areas of extreme tenderness over the

body, while numbness of the limbs, rheumatic pains in both the lower and upper extremities, congested conjunctivæ and retinæ, and defects of both sight and hearing are often present. The patient may complain of anorexia, insomnia, chills, and frequently talks about malaria as the cause of his symptoms. The urine is likely to be of high specific gravity, and to show albumin and an excess of phosphates. Chronic catarrhal conditions of the pharynx and larynx, dilatation of the skin vessels, sometimes pustular eruptions, are other early symptoms often seen.

At a later period the symptoms are more likely to point to certain structures of the body upon which the alcohol has exerted its chief effect. They may be grouped as follows:—

(1) *Digestive System.*—Chronic gastritis is a very frequent result of alcoholism. The patient complains of anorexia, nausea and vomiting, acute pain over the stomach, and constipation. The breath is foul and the tongue coated. These symptoms, usually most marked in the morning, the subject finds to be best relieved by further use of alcohol. The relief is but temporary, however, and when it ends the difficulty is increased.

Long-continued alcoholic intoxication produces in some cases pronounced structural changes in the liver, most frequently cirrhosis, with contraction of the organ, or fatty infiltration, with increased size. The symptoms of the former are those of chronic catarrh of the stomach and intestines (anorexia, nausea, flatulence, constipation, sometimes light-colored stools),—which is favored by the congestion caused in these organs through compression of the portal vessels,—together with others directly due to the same condition, such as hemorrhages from the lower esophagus, nose, pharynx, or even the stomach or intestines; hemorrhoids; distention of the veins of the face, especially the nose, or of other portions of the body, usually combined with flushing due to overfilled capillaries; occasionally jaundice. Later there may appear ascites, edema of the right pleura or of the lower extremities. Enlargement of the spleen is common late in the disease. Fatty infiltration of the liver produces no such distinctive symptoms, since there is no portal obstruction. The organ shows a moderate increase in size, but its functions are not markedly altered.

Fahr reports a series of 309 autopsies performed at the Hafenkrankenhaus (harbor hospital) of Hamburg on victims of chronic alcoholism dying from either alcoholism alone or from other causes, no less than 98 being suicides. In nearly all the cases the alcohol had been taken in the form of spirits, not as beer or wine. The results of these autopsies are distinctly not in harmony with the conception that alcohol is a poison which produces widespread and gross anatomic changes throughout the body, or that it is a common cause of either arteriosclerosis or nephritis. Even cirrhosis of the liver is far less common in alcoholics than it is usually supposed to be, for, of the 309 cases, in but 11 was cirrhosis the cause of death; in 2 other bodies there was an advanced cirrhosis, but death was due to some other cause. Of 100 cases of cirrhosis in which autopsies were performed by Simmonds in Hamburg, alcoholism could be excluded in 14; in 60 it was evident, and in 26 there was no reliable information as to alcohol; therefore, it must be concluded that, while only a very small proportion of drunkards suffer from cirrhosis (about 4 per cent.), there are not a few cases of advanced cirrhosis which are not due to alcoholism, although alcohol is

responsible for far more than a majority of all cases of cirrhosis. On the other hand, in nearly every case of habitual drunkenness the liver shows fatty changes, usually severe, but not ordinarily associated with connective-tissue increase, and this is by far the most frequent change in alcoholism. Editorial (Jour. Amer. Med. Assoc., Nov. 27, 1909).

(2) *Nervous System.*—In many cases alcohol acts most prominently as a motor paralyzer, the control over the muscles being greatly impaired. The hands are unsteady in their movements, and protrusion of the tongue is imperfect. Ultimately paralysis is a possibility.

Of 500 alcoholic cases examined, a considerable number showed no tremor. A moderate trembling of the hands does not necessarily point to an abuse of alcohol. In about one-half of the writer's cases, a tremor was noted which had no relation to the use of alcohol. A slight tremor is more often seen in total abstainers and moderate drinkers than in excessive drinkers. Women show a greater tendency to tremor than men. Fürbringer (Berl. klin. Woch., May 22, 1905).

In other cases cerebral symptoms are especially marked, the prolonged action of the narcotic having caused a gradual loss of mental power. Normal cerebral activities are replaced now by exhilaration, again by depression. The subject becomes sluggish mentally, weak morally, and loses in memory and will power. He may also show great irritability, or be in a continuous state of excitement. His ideals are changed, and egotistic tendencies appear. Later, evidences of abnormal cerebration may occur in the form of varying delusions and delirium. Permanent dementia is the terminal stage in this morbid chain of events, the patient becoming in his delusions timorous, suspicious, and sometimes grandiose. The symptoms of simple or multiple neuritis are also very frequently seen in cases of alcoholism, occasionally to the extent of permanent local paralysis (see Alcoholic Neuritis under Neuritis).

If carefully sought for, various forms of insanity following the use of alcohol can easily be distinguished from the ordinary intoxications. In favor of insanity are: A neurotic family taint; slight changes in character and disposition, especially moral and ethical changes; periodicity of the drink habit, weakening of the memory and of the will, a tendency to excessive anger, and periods of depression. A point of great significance, the writer believes, is the fact that occasionally, after the withdrawal of the whisky, there will appear periodically a condition closely resembling that of intoxication. This he regards as a sure sign of mental change, which should be treated by restraint of the patient for a long period. The author makes a strong plea for State provision for the cure of dipsomania. Dunning (St. Paul Med. Jour., Sept., 1903).

Alcoholic insanity presents special characteristic features which it is not difficult, in the majority of cases, to distinguish from other analogous conditions. Acute cerebral alcoholism presents 3 states: delirious, confusional, and stuporous. The intensity of these states varies according to whether we deal with a subacute form or with delirium tremens.

The chronic form leads inevitably to dementia. In the course of development of the latter, delusions with hallucinations and illusions may and may not manifest themselves.

In the latter symptoms it may sometimes present a picture of any other psychosis; this resemblance is only apparent, as in the majority of cases close observation will enable us to find the proper interpretations.

If the symptoms characteristic of cerebral alcoholism sometimes de-

velop in individuals affected with other psychoses who happen to commit excesses, or do so because of the perverted mode of thinking or feeling caused by the psychoses, it does not follow that alcohol is capable of producing these psychoses. The conception of alcoholic melancholia, mania, paranoia, or paresis is unscientific. Alfred Gordon (Jour. of Inebriety, Winter, 1908-9).

(3) *Circulatory System.* — Alcohol causes irritation of the intima of the vessels and gradual degeneration of the vascular walls. The symptoms produced are those usual in widespread arteriosclerosis: vertigo, hemorrhage or thrombosis of the cerebral vessels, etc. The heart and kidneys are very likely to be involved as a result of the same changes and undergo corresponding alterations in function.

In some instances the heart seems seriously affected. The patient complains of distress and pain over the precordial region, with alternate feelings of exhaustion and exhilaration. The pulse is frequent, and surface congestion is very intense. The heart may become dilated.

(4) *Kidneys.*—Chronic parenchymatous nephritis is not uncommonly caused by prolonged alcoholic excesses. Its manifestations include disorders of digestion, increased vascular tension, anemia with characteristic translucent pallor, tendency to swollen face and extremities, together with more or less distinctive changes in the urine. The latter consist of abnormalities in quantity (at first diminished, later increased), lower specific gravity, albuminuria; granular casts, sometimes fatty; epithelial and waxy casts, and decreased proportion of urea. The late symptoms include marked weakness, general anasarca, dyspnea on exertion, and uremia.

From a clinical study of 460 cases of chronic alcoholism the writer concludes that alcohol when taken daily, as it is by chronic inebriates, dipsomaniacs, or drinkers, is not an irritant to the kidneys. When nephritis occurs in a chronic alcoholic, it is probably due to some other concomitant toxic agent, and not to alcohol. Overeating, acute intoxicants, exposure to colds, autointoxications, infections either manifest or latent, and some metabolic disorders as yet unknown are the real causative factors of nephritis.

Alcohol when taken by drinkers as food or stimulant, such as seen in chronic alcoholism, is a diuretic. Those tissues which eliminate alcohol are least affected by it. This applies to the lungs and especially to the kidneys. While an intoxicant, alcohol is also a detoxicant, ridding the body of various deleterious catabolic products.

The comparative integrity of the kidneys in alcoholics may be due to the fact that the renal cells contain very few lipoids and lecithins, and that, therefore, they are not at all acted on by the narcotic molecule. J. F. Hultgen (Jour. Amer. Med. Assoc., July 23, 1910).

DIAGNOSIS.—This is facilitated if a history of excessive use of alcohol —at times in the form of proprietary remedies—be obtainable. If not, alcoholism is suggested by the presence of symptoms such as those given in the beginning of the section on symptoms, these representing mainly functional derangements and toxic effects, but few of them being the results of organic alterations. Active treatment is then begun. Under rest, restricted diet, and hydrotherapeutic measures many of these symptoms disappear, leaving only those expressive of permanent lesions.

Quinquaud's sign consists in a series of quick tappings or the sensation of slight shocks made by the phalanges when the patient's fingers are spread apart and extended and pressed perpen-

dicularly against the palm of the experimenter. It is only after a few seconds that the phalangeal shock is felt, and then only in case the subject is an alcoholic. Maridort (La méd. moderne, July 18, 1900).

The writer has investigated Quinquaud's symptom in a large number of cases and concludes that the crepitation does not come from the joints, but results from slight lateral motions of the tendons in their sheaths, set up by the involuntary muscular contractions so common in alcoholics. The symptom is present to a slight extent also in normal individuals. M. Herz (Münch. med. Woch., May 30, 1905).

Of 14 total abstainers, ranging in age from 22 to 35, 10, or 71.3 per cent., showed Quinquaud's phenomenon, which was well marked in 50 per cent. In a group of 25 moderate drinkers the phenomenon was present in 14, or 56 per cent.; very marked in 28 per cent. Minor (Berl. klin. Woch., May 6, 1907).

A careful re-examination at the end of two or more weeks will now indicate how many of the symptoms were functional, and which of them seemingly were organic departures from health. The special effects of the alcohol on particular organs or systems of the body are ascertained by noting the presence of symptoms referable to them, such as have already been mentioned under that heading. It must be admitted, however, that in many cases the symptoms will appear very complex and refer to no particular seat of organic disease.

At this second examination the diagnosis of the patient's psychic state can also be made with some accuracy. This should comprise a study of the patient's powers of reasoning, of his ideals, of his ethical conceptions of life, of the end and object in living, of his purposes and ambitions, of the effects of losses and mental strains on his character, of the dominance of certain passions and unrestrained emotional activities, and of the presence of morbid impulses and egotism. The inquiry should extend to the everyday habits of the patient. Not infrequently periods of unexplained absence from home and business, and of unexpected and obscure conduct, will be revealed. Such occurrences justify the inference of the paroxysmal use of alcohol. Often the pronounced convictions of the patient as to the cause of his condition are significant of the use of spirits, which he denies. The diagnosis can then be made with great clearness not from what he says, but from the facts he conceals or appears to be trying to cover up.

Material assistance will sometimes be derived from a study of the family history and past medical history. Hereditary tendencies, the diseases of childhood, profoundly exhausting fevers, and injuries to the body may all be of importance in reaching a decision.

The heredity element in inebriety is considerable and is undoubtedly a powerful predisposing cause in inebriety. A history of decided intemperance in the parents existed in over 40 per cent. of the writer's 700 cases, while 15 per cent. gave a history of defective ancestry, insanity, neuropathy, drug addiction or tuberculosis being present on the maternal or paternal side. Approximately 5 per cent. of the patients showed pre-existent mental symptoms which could be differentiated. Some of these were distinct cases of psychasthenia, others were of the milder forms of manic-depressive insanity. Neff (Boston Med. and Surg. Jour., June 16, 1910).

The influences and conditions surrounding the subject at the period of puberty, the effects on him of losses and failures early in life should likewise be ascertained, since they may have a

marked bearing on the establishment of vicious habits. If alcohol has been taken, no matter how moderately at first or at what long intervals, its influence upon subsequent morbid developments should be given due consideration.

Where the symptoms are complex and the diagnosis obscure, it is usually safe to give prominence to alcohol as a causative factor. In many such cases alcohol is used to conceal the taking of other drugs. The diagnosis can then only be a tentative one, the strong probability of an alcoholic neurosis being, however, kept in mind. It may have to be altered at any time upon the discovery of new facts in the patient's history or in his present condition.

PATHOLOGY. — In this are included changes in a large number of organs and tissues. It has been shown, indeed, that alcohol has destructive effects on protoplasm in general. Hence, cellular elements of all kinds are open to its action, though it has been recognized that it is the most highly differentiated cells, such as those of the nervous system, which are the most easily affected. Its influence on the cells is exerted by reduced oxidation and altered metabolism. Destroyed cells, in virtue of a low-grade inflammatory process it produces, are replaced by connective tissue. The effect of alcohol in diminishing oxidation is most prominently expressed in the failure to oxidize fats normally, with consequent accumulation, as in the liver and subcutaneous tissues.

> Distinction made between the diffuse, irregular spinal cord changes brought about by alcohol and the more systematized processes. The diffuse changes consist in a thickening of the vessel walls and increase in the connective tissue of the pia and of the cellular tissue surrounding the cord, hyaline degeneration of the small vessels, and a diffuse gliosis, which destroys the nerve-fibers. The changes are not different from those found in arterial sclerosis and marasmus. Commonly the changes are most marked in the posterior portions of the cord. The more symmetrical changes are found in the posterior column, with projections into the posterior roots, especially marked in the lumbar enlargement. This was frequently associated with changes in the peripheral nerves. The changes could not be distinguished from those of beginning tabes. E. A. Homen (Zeit. f. klin. Med., Bd. xlix, H. 1-4, 1903).

PROGNOSIS. — This is generally very favorable. Statistical studies in well-conducted institutions show that at least one-third of all the cases are permanently restored. The statements that 90 per cent. are cured have reference to present conditions, and are probably true for a limited time. On the turn of the drink cycle relapse occurs, and later recovery.

Statistics of cure are unreliable. In the treatment by gold chloride 95 per cent. were claimed to be cured. At the end of one year after treatment 55 per cent. had relapsed. At the end of the second year another 20 per cent. began to drink again. In the third only 10 per cent. continued temperate and free from spirits. On the other hand, at Binghamton, N. Y., where the first exhaustive study was made of the subsequent history of 1100 patients, ten years after they had been treated, the results showed 61 per cent. still temperate and well. These and other statistics, while open to error, clearly suggest that at least 33⅓ per cent. may be reasonably considered permanently restored.

The future of the inebriate depends

largely on the removal of the exciting causes, whatever they may be, and their avoidance in the future. In a certain number of cases there is a complete cessation and physiological change in the organism in which the impulse to use spirits passes away forever. This is now well known. It cannot be predicted, but it occurs so often that we cannot but credit the results to greater knowledge, and to the use of more exact means in the treatment.

It may be stated that the prognosis is always good, even in cases that have apparently reached the terminal stage. This prediction refers specifically to the craze for alcohol. This dies out, is overcome by drugs and rational treatment, while other conditions of degeneration may remain.

The alcoholic or inebriate is a compound of a great variety of causes, the removal of which brings about cure. Sometimes those causes are very insignificant, sufficiently so, in fact, to be readily overlooked.

TREATMENT.—This resembles the prognosis in uncertainty and wide variations, indicating beyond question that the subject has been scarcely touched. Both hospital and home treatment, and even moral measures, show examples of permanent restoration. The field is very wide and largely unknown.

Home Treatment.—First, there is the home treatment, *i.e.*, care given to the patient in his own home by the family physician. It is evidently possible to restore many persons, particularly if they give their full assent and co-operation and carry out the measures laid down for them.

Home treatment requires implicit confidence in the medical adviser, and should consist of the absolute withdrawal of spirits and the use of means and measures to restore and relieve the conditions of starvation and poisoning present.

While the causes differ in each case, their removal and the after-treatment are substantially the same. Thus, one whose living, both in regard to nutrition and rest, is bad requires a change. Nerve rest and regular diet must be a part of the treatment.

In one who has become poisoned by spirits and highly stimulating foods, the withdrawal of these agents and rest are essential. Probably **hydropathic measures** to insure elimination by means of the skin represent the most effective method of treatment.

Many of these patients are suffering from delusional egotism and inability to recognize their condition (constantly overrating their strength), and are unwilling to use the means so evident to others. The family physician should be dogmatic and exact the use of means and measures that will break up the impulse to use spirits. He should treat the patient mentally as well as physically, and the danger of the situation should never be minimized; he should not permit the patient to think that he can depend on his own will to overcome his diseased impulses. In many instances the patient is impressed with the gravity of his disorder. He must be urged to make radical changes in his living and conduct. If his work is indoors, a change to out-of-door life is requisite. If he has neglected proper exercise, this should be arranged for in some satisfactory way.

Everything that will change the present current of thought with mental and physical activity belongs to rational

treatment. Of course, with this, appropriate remedies and measures to neutralize and diminish exciting causes will suggest themselves to the physician. He should recognize that these are often border-line cases in which both reason and will are clouded and the patients are irresponsible. They need suggestion, forcible and emphatic; physical treatment, and persistent use of all therapeutic means. The family physician can do a great deal in this field if he will prepare himself for it and study the peculiarities of the patient.

Office Treatment.—This is equally promising in results where the patient is recognized by the physician and his condition understood. Drug treatment forms a very important part of the means to bring relief. Probably the most practical drugs are combinations of **strychnine** and **atropine,** given at short intervals for a few weeks, then replaced by some other agent.

> **Strychnine** is the physiological antagonist of alcohol, and when properly administered it will remove the appetite for alcohol. It will do this without detriment to the system in any respect, and usually with the greatest benefit. Other remedies may with advantage be combined or alternated with strychnine, especially **atropine** or **hyoscyamine;** but it is strychnine which does the lion's share of the work, and it can usually be done with strychnine alone. J. M. French (Merck's Archives, April, 1907).
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> Favorable report of treatment, essentially that first proposed by McBride, which consists in the hypodermic injection of **atropine** and **strychnine** twice or thrice daily for a month or six weeks, with attention to general hygienic condition, and tonics by the mouth. At the commencement of the treatment patients were told that its success depended on their regular attendance for injections. The writer reports 7 cases, all of them presenting marked degrees of alcoholism, which had been treated in this way. In 5, treatment was commenced in September, 1905; July, 1907; March, 1908 (2 cases), and July, 1909, respectively. These cases had remained cured up to date. In the 2 other cases relapses had occurred after two months and four years respectively. W. Asten (Lancet, Nov. 6, 1909).

The impulse to drink may be effectually controlled by small doses of **apomorphine** given hypodermically or by the mouth. Concentrated aqueous infusion of **quassia** given every hour very quickly breaks up the drink impulse, and frequently destroys the taste for tobacco, which is often a very important factor in the use of spirits.

In the office treatment care should be exercised not to substitute for spirits narcotic drugs that are likely to produce poisonous effects if taken without caution. Chloral hydrate is one of these drugs, commonly administered, but it is unsafe and dangerous; also many forms of opium and its derivatives.

Humulus is a narcotic of great power at times, and is often an excellent substitute for spirits. It is not wise to give tinctures to patients who come to the office for treatment. Give infusions always. **Salines** are very practical measures and can be given freely without risk.

Office patients of this class want remedies that will impress them at once; hence, the physician must study the drugs whose effects are more or less certain. **Sodium bromide** is a favorite drug, and can be used with safety; only, the physician must realize that it is cumulative in its action, and that **baths, cathartics,** and

diuretics are to be associated with its use constantly.

Office patients should be urged to take daily baths and **exercise in the open air**, but should be impressed psychically with the need of avoiding causes which lead or predispose to exhaustion. It is impossible to specify particular drugs and a plan of treatment applicable to every case.

The conditions vary so widely and the active and exciting causes depend on so many circumstances—surroundings, occupation, success or failure in life, diet and social influences, rest, etc.—that each case becomes a law unto itself, and requires a very close study of the conditions present.

Hospital Treatment.—This is far more successful, particularly in persons who have reached the later stages of degeneration. It is a common experience to have persons go to a hospital or sanatorium and recover from the immediate effects of spirits, and have a period of rest, change, and thorough elimination of the active exciting causes. They can then return to the family physician and remain under his care for an indefinite period. It often happens that hospital treatment and restraint is the only measure that has any promise of permanency. Such hospital treatment is effectual by combining hydrotherapeutics and sanitary appliances with hygienic measures specifically adapted to meet the wants of every person.

Drugs are very essential adjuncts and aid materially in restoring the vigor and metabolism of the body. Diet and exercise are also very important remedies. These, with nerve rest, change of thought and surroundings, are followed by restoration, and where these measures are continued over a certain length of time the cure is permanent.

The actively working inebriates and alcoholics who are carrying loads of responsibility need hospital-homes in the country or by the seashore where absolute rest and quietness can displace their usual unhygienic activities. The diet, exercise, baths, electricity, tonic drugs, new duties, and new conceptions of their actual conditions must be forced upon them and become a part of their everyday life.

Here **psychic therapeutics** comes in as a very important means of treatment, and as a supplement to other and physical remedies. A sanatorium hospital will supply these needs, afford a clear knowledge of the patient's condition, and train him in the conduct he should observe in the future.

> The writer divides inebriates into 2 classes, those whose will power is not destroyed, but only latent as it were, and capable of being revived, and those in whom it is hopelessly impaired. It is the first of these classes that furnishes the converts in the temperance revivals and the so-called successes of the various specifics or "cures" for alcoholism, and the good result here is not due to the medication, which acts indirectly perhaps as an aid to mental suggestion, but to the psychic stimulus and the environment. The conductors of the so-called "cures" are illogical in their use of remedies and, therefore, untrue in their assertion Their practice is irrational and unethical, and they are in no sense humanitarian. They should not have the protection afforded regular medicine, but should be brought under the laws regulating "patent" or proprietary medicines. There is no specific in the treatment of alcoholism or inebriety in the proper sense of the word. In a certain class of selected

cases it is proper to use **psychic treatment**, especially before complications develop and while the patient is still responsive. If the case is complicated with organic disease appropriate medical treatment should precede or accompany psychotherapeutic measures if the latter are deemed advisable. L. D. Mason (Jour. Amer. Med. Assoc., Feb. 23, 1907).

There are many hospitals and sanatoria with varied measures of treatment, but in none of those worthy of confidence are there any specifics enveloped with mystery. The treatment has passed beyond the empiric stage, and is now as thoroughly fixed with its positive results as that of any other disease, and there are no specifics or combinations of drugs that can effectually check the drink impulse unless at the peril of its breaking out again with greater force.

[A second class of hospitals should be organized on the workhouse plan, providing all the means and measures found best in the sanatorium with the addition of making labor a part of treatment. These would receive the indigent and the terminal cases, which would be sent there by process of law, and which would become more or less permanent residents. T. D. Crothers.]

GENERAL TREATMENT.—Every inebriate is toxemic, and every attack of drunkenness is a period of exacerbation of this toxemia. The first measure is to **withdraw the spirits** and remove the poison by stimulating the bowels and the skin to insure its elimination. **Calomel**, either in a large dose of 10 grains or a small dose of 1 grain every two hours, until 6 or 8 grains are taken, together with salines, are the most effective cathartics, and should always be used at the beginning.

If the patient objects to the sudden removal of alcohol, and his condition borders on delirium, $\frac{1}{10}$ of a grain of **apomorphine** hypodermically should be given as a relaxant. This will be followed by vomiting, free perspiration, and sleep. On awakening a **hot bath** of the temperature of 105° or 110° should be given. If the patient will consent to lie in the bathtub for an hour or two at a time, then be rubbed down and recline in a cool room, excellent effects will be obtained. If he will not, an ordinary hot bath should be followed by a vigorous hand rubbing and reclining in bed. If the desire for spirits continues and the depression is not marked, $\frac{1}{30}$ grain of **strychnine** with $\frac{1}{200}$ of **atropine** should be given every two hours.

To get a man on his feet with a clear brain, and with the craving for narcotics removed, a mixture of drugs given to the writer by Mr. Charles B. Towns has proven of value. It consists of a mixture of 15 per cent. **tincture of belladonna**, 2 parts, and 1 part each of **fluidextract** of **xanthoxylum** and **fluidextract of hyoscyamus.**

From 6 to 8 drops of this are given every hour, day and night, until either the patient shows symptoms of **belladonna** excess or, with the cathartics about to be described, the patient has a certain characteristic stool. This dose of the mixture is increased by 2 drops every six hours, until 14 to 16 drops are being taken; it is not increased above 16 drops. Usually an alcoholic can be given 4 compound cathartic pills (U. S. P.) at the same time that the specific is begun. After the mixture has been given for fourteen hours, a further dose of C. C. pills is given, either 2 or 4, depending upon the amount of action obtained through the use of the previous dose. If these have acted very abundantly, only 2 are now necessary. At the twentieth hour of the mixture 2 to 4 more C. C. pills are given, and after these have acted, should the patient begin to show abundant green movements, an ounce of

castor oil should be given, and a few hours later the characteristic thick, green, mucous, putty-like stool will appear. Usually the mixture has to be continued, and at the thirty-second hour 2 to 4 C. C. pills are again given, and a few hours later the castor oil. The mixture can then be discontinued.

Of course, in treating alcoholics, one finds in the majority of cases the necessity to stimulate them and to give them some hypnotic, but this can be done without interfering with the hourly administration of the above. Alexander Lambert (N. Y. State Jour. of Med., Jan., 1910).

The belladonna treatment properly given will totally eradicate the physiological craving for narcotic drugs, including alcohol. To secure permanent results it is necessary to pay as much attention to the after-care in both alcoholic and drug cases as is given to the derivative treatment. This after-care consists in regular supervision over several months and a thorough understanding of the needs of the patient by both himself and his friends. The treatment consists in the hourly administration of a mixture of **belladonna, hyoscyamus,** and **xanthoxylum,** in connection with increasing vigorous catharsis at stated intervals. At the end of this course a so-called "typical stool" is obtained, and the patient emerges into a very unusually comfortable condition with little or no craving remaining. There are several points to be noted about this vigorous derivative treatment. The belladonna mixture must be pushed to the physiological limit and not beyond. Atropine poisoning must be sighted, but not reached. To fall short of this point spells failure to actually obliterate the craving; to overstep it intimidates the patient. Ross Moore (So. Calif. Pract., July, 1911).

If the restlessness and excitement continue, repeat the **apomorphine** in $\frac{1}{20}$-grain doses every two hours. Should the stomach be irritable, use **hot and cold fomentations** over it, and give carbonated waters, usually **Vichy.** The patient should not take any food, for, as a rule, digestion is impaired to the extent that food cannot be assimilated.

If the patient is restless and insists on moving about, have an attendant go with him and walk him until he shows **fatigue,** then bring him back and give a hot tub bath or shower with **apomorphine** and **strychnine.**

Never give chloral or morphine. The latter may be used under special circumstances, but the former is contraindicated. For the insomnia **lupulin, valerian, cannabis indica,** and other vegetable narcotics may be given, but never in the form of tinctures.

Often some of these drugs produce sleep at once. Others have little or no effect and should not be given. The size of the dose will depend upon the apparent sensitiveness of the patient to the effects.

Occasionally, where there is a tendency to delirium, **bromide of sodium** in from 50- to 100- grain doses may be used. Not more than 3 or 4 doses at intervals of three hours should be given. After giving this drug the patient should take a hot bath, which has the effect of producing more rapid absorption of the salt. Sometimes a **salt bath** is preferable to plain water, if there is much depression.

Cinchona bark in infusion has a very good effect, and infusion of **quassia** chips is another remedy of great value, but for the acute stages hot water, hot baths are most practical. In the course of a day or so a disgust for spirits begins. In the mean time **salines** should be given and the bowels kept loose.

The **strychnine** combination should be kept up, and should the **atropine** symptoms appear the size of the dose diminished. Food should be taken very sparingly for the first two days. After that a diet rich in **cereals** and **malted milk** may be given.

As a rule, milk is not a good diet for these cases. **Coffee** and **tea** may be used according to the taste of the patient. **Exercise** in the open air and reclining in a cool room, with nerve rest, are very essential.

The disposition of the patient to eat inordinately should be suppressed. If there is a tendency to constipation, mineral waters that are laxative on an empty stomach should be given.

> **Caffeine** is almost a specific in alcoholic toxemia. This drug in doses of 1 to 2 grains every one, two, or three hours will usually, in from twenty-four to forty-eight hours, quench the thirst or craving for alcohol to such an extent that the most confirmed habitués will voluntarily abandon its use. Four cases are reported which seem to uphold the author's contention. Hall (Med. News, Oct. 31, 1903).

Elimination through the skin, bowels, and kidneys should be the main purpose of the treatment, all with proper nutrition and rest. Where there is a history of specific disease, **mercury** or **arsenic** in small doses is required. When the paroxysm subsides and the patient is restored, the great question becomes to determine the exciting causes which produce the return of the drink craze, and ascertain their periodicity.

In most cases it is wise to discontinue the strychnine compound and continue the free use of baths, carefully regulated diet, with salines, for some time, until evidence of the return of the drink craze appears.

If the patient keeps in close touch with the family physician his digestion, nervous symptoms, and habits of living can be studied and properly treated. Where possible, **Turkish baths,** with **prolonged rest** afterward, should be given at least once or twice a week.

If the physician can secure the full confidence of the friends as well as the patient, and impress upon him the necessity of extraordinary care and the methodical use of hydropathic measures, a great deal can be accomplished.

In the country, baths may be improvised in a tub, and water falling on the patient in a narrow stream has an excellent sedative effect. **Hot packs** or sheets wrung out in hot or cold water covering the body, over which are spread dry blankets, producing intense or rapid perspiration, are often most valuable.

The physician should always study the digestion of the patient and determine the states of acidity or alkalinity of the stomach and correct them as required.

Exhaustion and depression frequently precede a drink impulse. Small doses of **ipecac,** ¼ of a grain given at intervals of two hours, produce a pronounced relaxing effect, and where the patient has high-tensioned arteries and excitable pulse this is an excellent remedy.

Quassia chips in a concentrated solution are almost a specific for the drink craze, but they must be given in large doses at intervals of an hour or so, and followed by free use of cathartics and baths. **Quinine** has some value, particularly where there is a history of malaria, but it should not be used more than two or three weeks.

All such cases are self-limited and will recover with the use of hygienic measures. The great value of the physician is to determine and remove the causes and, where there is a periodicity in the return of the paroxysm, to have the patient under treatment and anticipate this condition.

The nervous disturbance of drug habitués depending upon the disturbance of the vascular system, the indication is to bring about promptly an equilibrium of the circulation, and for doing this the hypodermic injection of **ergot** is the most certain method. Ergot contracts the muscular coats of the blood-vessels, but its most pronounced action is upon areas of such tissue as is weak and relaxed, and, hence, its action on dilated blood-vessels is peculiarly satisfactory. The first step in the treatment of these drug habits is to discontinue the use of the narcotic, or of any substitute therefor. The use of ergot is begun at once, giving a purgative at the same time, and the bowels are kept open. In general, 2 or 3 doses of ergot of ½ dram each of a solution consisting of 1 dram of the extract dissolved in an ounce of water are given daily, but in extreme cases it may be necessary to employ the drug at intervals of two hours. The ergot method acts admirably in the morphine habit, the most difficult of all to cure. A. T. Livingston (Merck's Archives, Nov., 1903).

The writer carries out the "gold cure" for alcoholism in the following manner: The patient is put under the pleasantest surroundings, no restraint whatever is used, and he is allowed all the alcohol he wishes. **Atropine** (or daturine) and **strychnine** are given hypodermically, and a mixture of **chloride of gold and sodium, ammonium chloride, aloin, viburnum,** and **cinchona** is given every two hours during the day. By the fifth day the patient voluntarily abstains from alcohol, and at the end of four weeks the drink-sodden victim of intemperance is transformed into a healthy and sober man. The treatment is necessarily institutional from its very nature. Of the author's patients he estimates that 60 per cent. remain total abstainers. Fenn (Brit. Med. Jour., April 30, 1904).

The treatment of drug and alcohol habitués with **hyoscine** will remove the desire for these drugs, thus eliminating the element which prevents the patients from abstaining by force of will power. Having lost the desire, they do very well without intoxicants or the drugs, as shown by the increase in appetite, gain in flesh, and their general improvement. The question of relapse lies entirely in the sincerity and environment of the patient. The favorable alcoholic addicts are those who earnestly desire to discontinue the use of intoxicants and are willing to change their mode of living and environment, but who cannot until relieved of the craving for liquor. Relapse in both drug and liquor cases is not due to a desire nor suffering after the treatment, but to their curiosity to test the necessity of total abstinence, or to the temptations of social life. A single dose of the drug or drink of liquor, even after one year of total abstinence, is very apt to start the craving, resulting in a condition which is no better than before treatment. This method may prove a valuable treatment in apparently hopeless cases of opium poisoning. Interesting experiments along this line might be carried out. The one contraindication for this treatment is the presence of Bright's disease. No patient should be treated unless put to bed and watched by competent nurses day and night during the first week. Riewel (Monthly Cyclo. and Med. Bull., Oct., 1909).

In delirium opium and its derivatives and many of the other drugs that are powerful narcotics should be avoided. All proprietary drugs are dangerous, and should be condemned no matter what the experience may be. Every physician is capable of doing far more for the relief of this con-

dition by adapting the remedies to the particular case than by any widely exploited compound.

[Workhouse hospitals for inebriates are just being recognized and will take the place of the present ruinous jail and fines system of the courts. Nothing is more unscientific than treating the inebriate as a moral delinquent and punishing him as though sound and capable of doing otherwise.

All physicians should protest vigorously against this relic of barbarism, and insist that the alcoholic be cared for in hospitals, the same as any other sick person. Everywhere a new field of practice is evident, and the possible restoration of a large number of the drink and drug takers is absolutely certain from a larger knowledge and more exact study of their conditions.

The important fact should be recognized that at least 70 per cent. of all inebriates and alcoholics are of the defective, degenerate classes whose conditions are the result of causes pronouncedly physical and preventable with more exact study and knowledge. The remaining 30 per cent. are the victims of circumstances, surroundings, and conditions which are equally preventable. In this field there are possibilities of successful treatment and prevention that will exceed all expectations. T. D. Crothers.]

ACUTE ALCOHOLIC DELIRIUM, OR DELIRIUM TREMENS.

This is a condition of acute alcoholic poisoning, associated with exhaustion and cell starvation. It occurs chiefly in habitual drinkers, but it is also observed in ordinary temperate persons after a prolonged drinking spell. Though mostly met with in spirit drinkers, it is occasionally seen in beer, wine, and cider drinkers.

SYMPTOMS.—Two forms are distinguished: the *traumatic* and the *idiopathic*. They differ little except in the prodromata. In the traumatic form, after an accident (sometimes only slight trauma) the characteristic tremors, etc., appear, frequently without warning. In the idiopathic form, the patient who is about to have an attack is restless, uneasy, irritable; he sleeps badly, if at all, suffers from digestive troubles, and has little desire for food. Delirium then appears. The patient cannot rest, but must be in constant motion. He is shaking all over ("the shakes"), is consumed with terrors, continually in deadly fright of things which he mentally sees, or of persons whom he thinks are after him for the commission of some crime. At other times his dread is of something terrible, though he cannot tell what it is. He is all the while trying to escape from these well-defined or undefined horrors, and, in the attempt to escape, fatalities sometimes occur. Hallucinations of sight are most common: snakes, rats, mice, loathsome things, flames, and, in a case of the writer's, roaring lions bounding down the chimney, below the chairs, and rushing in at the windows. According to Liepmann, visions of animals are present in 40 per cent. of cases at most. The delirium is best described as one of busy wakefulness and suspicion. There is a third non-febrile, innocent form, in which the temperature does not rise above 100° F.

Hallucinations of hearing are not so common, but exist in probably 10 to 20 per cent. of cases. Delusions (false perceptions concerning self) are found in from 5 to 9 per cent.,—mostly delusions of persecution. Sometimes there is one hallucination, illusion, or delusion throughout; sometimes there is a succession.

The tongue is white and furred. Tremor of this organ, and especially of other muscles, is a more or less marked and generally present symptom.

The fever is not very high, being about 100° to 103° F. If higher, it is an unfavorable omen. The pulse is soft, rapid, and readily compressed. The skin is clammy. Insomnia is constantly present, but usually sleep and improvement occur on the third or fourth day. In unfavorable cases the patient grows gradually worse and dies of heart-failure (Norman Kerr).

Analysis of the material of the Moscow Clinic as regards the statistics of alcoholic delirium. Only cases of chronic alcoholic delirium in which the presence of insanity of any other type could be excluded were utilized. Out of 4813 insane registered in the clinic since its opening, it was found that there had been 33 cases of chronic alcoholic delirium. Of these, 30 were in men and 3 in women. Of 29 cases in which the heredity was noted 20 showed alcoholism in the parents, principally in the father; 3 patients showed nervous or mental diseases in the immediate family. Heredity was, therefore, present in 96.55 per cent., and these figures, according to the authors, showed conclusively enough the hereditary nature of chronic alcoholism. So far as the small number of cases observed warrants a conclusion, chronic alcoholic delirium develops much later in life in women than in men, and this is because the women begin to abuse liquor much later than men. Soukhanoff and Vvedenski (Roussky Vratch, July 12, 1903).

Case of death from delirium tremens after a slight fall which without this complication would have been comparatively harmless. The spontaneous pain of the contusion subsided under repose by the second day, but then delirium tremens developed, fatal on the sixth day. The writer has witnessed a number of cases of this kind and discusses the question from the standpoint of accident insurance. There can be no question as to the connection between the accident and the development of the fatal complication. Forgue (Presse méd., July 24, 1909).

Delirium tremens, other conditions being equal, attacks males and females alike. The greatest number of cases was found at an age between 31 and 45 years. A congenital psychopathic diathesis is not uncommon in patients having delirium tremens. Epilepsy is extremely frequent as a sequela of alcoholism, and was repeatedly noted in these cases. There are numerous epileptics from abuse of alcohol, however, who never develop delirium tremens; and on the other hand, many individuals suffering from delirium tremens have never had an epileptic seizure. Epilepsy was noted in 43.66 per cent. of the delirium tremens cases. Among 284 cases observed by the writer, there were 27 deaths, 9.5 per cent. The principal danger is of heart-failure, and in these cases there is no objection to the medicinal use of alcohol. Wassermeyer (Archiv f. Psychiatrie, Bd. xliv, 1909).

DIAGNOSIS.—Alcoholic delirium may be mistaken for the delirium of meningitis, of typhus and typhoid fevers, and of chronic alcoholism. The history and progress of the case determine the first two, and the absence or significance of thirst, tongue trembling, and tremors the third.

Pulmonary disorders; congestion, especially when of traumatic origin, and pneumonia may also give rise to delirium simulating that of delirium tremens. Fractured ribs may thus become the primary factor of violent accesses. The same may be said of erysipelas.

PATHOLOGY.—Acute alcoholism is due to gradually produced changes in the nerve-tissues, and especially to retained products of metabolism. The cerebral lesions in alcoholic delirium are of two varieties. The first is observed in all alcoholics, and is due to the alcohol itself: atheromatous de-

generation of the vessels, the degree of disorder increasing as the caliber of the vessel is reduced. The nerve-cells also show granular pigmentation and fatty degeneration.

The second variety is derived specially from the character of the delirium, and not from the alcohol itself. It consists in congestion, hematic pigmentation in the capillaries and nerve-elements, and degeneration of the nerves and fibers of the cortex, the precursors of general paralysis (Norman Kerr).

According to Jacobson, delirium tremens occurs when a brain, deteriorated by chronic alcoholism, is influenced by a toxic agent, either due to the action of bacteria or to autointoxication from diseases of the digestive tract, the kidneys, or the liver.

The changes in the central nervous system and spinal ganglia are quite uniform; they consist essentially, first, in thickening of the walls of the arteries, proliferation of the connective tissue in the media, and dilatation and infiltration of the lymph-spaces. These changes are more pronounced in the cortex, and frequently lead to minute hemorrhages, as many as 200 of these having been counted in a square centimeter of the cortex. The capillaries appeared to be proliferated, particularly in 1 case, but they and the veins showed no pronounced anatomical alteration. The neuroglia fibers of the cortex showed, according to Weigert's new method, considerable proliferation. The Weigert cells were more numerous than normal. The free nuclei, both the small and large varieties, were increased in number in the second and sixth layer of the cortex, and appeared to be accumulated around the degenerating cells. The spinal cord was apparently normal (Tromner).

Of 247 recovered personal cases of delirium tremens studied by Jacobson, 202 were uncomplicated and 45 complicated by other diseases. Although the delirium tremens cannot be regarded as caused by the action of the pneumococcus, it resembles, in all its features, an infectious disease: it has a stage of incubation—a duration of about four days; it ends with a critical sleep; is accompanied by rise of temperature, and almost in all cases by albuminuria, and when autopsy is made the spleen is generally found to be the seat of parenchymatous degeneration, as well as the heart, the kidneys, and the liver.

PROGNOSIS.—In private practice the prognosis is favorable in ordinary cases; in hospital practice it is much less so. Of 1241 cases admitted to the Philadelphia Hospital during a fixed period, 121 died. Recurrence occurs if drinking is continued. Norman Kerr noted recurrence from one to five times in 104 out of 442 cases treated in a special institution.

TREATMENT.—The first indication is to **remove the causative toxemia**; this can be done by persistent and active **hydropathic measures.** Hypnotics are not always necessary, and may be dangerous. They should be avoided if possible. The best treatment is continuous baths, showers, salines, restraint, exercise, massage, good air, and little or no food until the delirium subsides. The following represents, however, the measures generally recommended in such cases:—

The patient must be kept in bed and carefully watched. Strapping in bed should not be practised, as the restraint causes muscular movements and delirium. A sheet tied across the bed is preferable, as this allows more freedom of motion. Attendants or a

padded room is best of all. **No alcohol** should be given, the strength being sustained by foods, milk, soups, etc.

> The **immediate suppression** of alcohol in delirium tremens and the employment of **hydrotherapeutic measures** advised rather than of hypnotics; the former serve to increase and to maintain the activity of the heart, although one would expect an opposite effect. In instances of cardiac weakness stimulants, **strophanthus, digitalis, camphor, caffeine,** are employed, and in about three days, when the delirium begins to lessen, 30 to 60 grains of **chloralformamide** are given; this quickly induces sleep. Thirst is controlled by bitter infusions. If pneumonia appears as a complication, digitalis and alcohol are administered. In these patients the prognosis is distinctly bad. Eichelberg (Münch. med. Woch., Bd. xx, S. 978, 1907).

Potassium bromide, ½ dram, with tincture of capsicum given every three hours, is recommended for mild cases by Osler.

Sleep is, however, deemed necessary by some authorities. According to Lancereaux, for example, the real chance of recovery in alcoholic delirium lies in **sleep.** The patient is, therefore, isolated in a quiet, dark, and, if necessary, padded room, no physical restraint being employed. To procure sleep the patient is given 1 to 1½ drams of **chloral hydrate,** with ½ grain of hydrochlorate of **morphine,** in an infusion of limes. If sleep does not come on in about ten minutes, from ⅙ to ¼ grain of **morphine** is injected hypodermically. After the alcoholic disturbance has subsided **strychnine** or **nux vomica** is given, followed by **hydrotherapeutic measures.** If there should be gastric complication, an antacid, such as **sodium bicarbonate,** is administered.

The author describes the treatment that he uses in cases of delirium tremens. The patient is stripped naked and lies on a blanket over a waterproof sheet. A copious supply of ice-cold water is provided, and a large bath sponge dripping with the iced water is dashed violently on the face, neck, chest, and body as rapidly as possible. He is then rubbed dry with a rough towel, and the process is repeated a second and a third time. The patient is now turned over, and the wet sponge is dashed on the back of the head and down the whole length of the spine two or three times, vigorous friction with a bath towel being employed between the **cold-water applications.** By the time the patient is dried and made comfortable, he will be fast asleep. William Broadbent (Brit. Med. Jour., July 1, 1905).

The writer reports the result of five years' use of **veronal** in delirium tremens. His method of administration is as follows: An initial dose of 1 Gm. is given in all incipient cases. If sleep does not follow within three hours, another gram is given. Sleep then follows and lasts six to eight hours, or even twelve. On waking the patient is clear, quiet, and feels well. If there is yet some tremor, 0.5 Gm. of veronal is given, and by evening all tremor has, as a rule, disappeared. If the patient remains in the hospital some time longer for other reasons, 0.5 Gm. is given every evening to insure against sleeplessness. If the delirium is not controlled from the 2 Gm. as given above, another gram may be given five to six hours after the second dose. Only 3 patients have failed to respond to this treatment out of a total of 100. There were 2 deaths from double pneumonia. In all the author's experience he has only seen 1 case of veronal rash, and absolutely no other symptoms of veronal poisoning. V. F. Möller (Berl. klin. Woch., Dec. 27, 1909).

Delirium tremens, on alcoholic basis, even in strong men of middle age, is a serious illness, with a mor-

tality variously stated as 3 to 19 per cent. The writer treated 396 cases from 1901 to 1906 with **chloral hydrate** (1 to 3 grains) and with **bromides. Digitalis** was given only when necessary, and alcohol was withheld. The mortality was 9 per cent. Of the cases, 17.4 per cent. belonged to the type of delirium imminens. Between 1907 and 1909, 264 cases were treated almost exclusively with **veronal.** The drug was dissolved in warm tea. Soon after admission the patient received 1 Gm. (15 grains), and one to two hours later a second gram. If necessary, a third gram is administered within five hours and a fourth gram within twelve hours. There never was the slightest untoward effect on pulse or respiration. The mortality sank to 3.4 per cent.; the percentage of cases where the delirium could be prevented rose to 28. The majority of fatal cases already suffered from pneumonia. This observation proves that veronal is far superior to chloral and bromides to check the attack in its incipiency, and also to prevent a fatal issue. Ernst v. d. Porten (Therap. d. Gegenwart, June, 1910; Merck's Archives, Nov., 1910).

Incipient cases, with insomnia, restlessness, tremor, occasionally hallucinations, should receive large doses of **hypnotics,** preferably **veronal; whisky** should be given regularly, and **ergot** at frequent intervals, either by intramuscular injection or by mouth. Discontinue medication *gradually,* and only after all restlessness and tremor has disappeared. More advanced cases, with marked delirium, incoördination, usually fever, slight leucocytosis, and profuse perspiration, should receive **veronal** in moderate doses; also **ergot.** Ranson and Scott (Amer. Jour. Med. Sci., May, 1911).

It must not be forgotten, however, that large doses of narcotics, with the cardiac depression apt to follow their exhibition, are dangerous, especially in the aged and infirm inebriates. Kerr preferred repeated doses of **liquor ammoniæ acetatis** (B. P.). Sleep, thus quietly and safely induced, has proved much more curative than narcotics in his practice.

Trional and **opium,** if given, should be administered cautiously.

If fever is present, the **cold douche, bath,** or preferably the **wet pack** may be tried. If the pulse becomes too rapid and weak, very small doses of **digitalis** in **aromatic spirit of ammonia** should be given. **Digitalis** in large doses is dangerous (Osler, Delpeuch, Kerr).

The author witnessed the collapse and death of a robust man in delirium tremens while being given a prolonged warm bath. One of his patients succumbed in collapse during a wet pack, and he has consequently abandoned these measures. In treatment of 1051 cases of delirium tremens in the last sixteen years, he has made it a rule to allow no alcohol. In the first series of 486 cases the mortality was 6.37 per cent., while in the last 565 cases it has been only 0.88 per cent. He ascribes this improvement in the results to his observation of the fact that the cause of death in delirium tremens is generally paralysis of the heart, and he now addresses treatment to the heart regardless of whether cardiac symptoms are apparent or not. The agitation and motor excitement react on the heart, and signs of heart weakness soon become manifest. He makes it a rule to give **digitalis** from the very first, giving 1.5 Gm. in an infusion in the course of the day and repeating this dose two or three times. If it cannot be given by the mouth, he gives it in a rectal injection. At the first signs of heart weakness other heart tonics are used; 1 Gm. of **camphorated oil** is injected subcutaneously every hour or so until the critical symptoms subside. A tablespoonful of ice-cold **champagne** every half-hour was also found useful—the only way in which he allows alcohol. To promote the washing out of the toxins causing

the attack, he has the patients drink copiously, and supplies them for the purpose with a drink which has the color of beer and tastes refreshing, and is taken eagerly by the delirious patient. It is merely a 1 per cent. solution of **sodium acetate in water** to which a little common syrup has been added. S. Ganser (Münch. med. Woch., Bd. liv, Nu. 3, 1907).

The writer ascribes the symptoms of this condition to the accumulation of toxic products, autogenous as well as alcoholic, in the blood. Accordingly, he aims at the removal of these deleterious substances. He gives **normal salt solution** in large quantities by the rectum, hypodermically, or, if necessary, intravenously. Thus the entire circulatory system is flushed with fluid to its utmost capacity, and this is then relieved by free purgation with large and repeated doses of **Epsom salt**. **Calomel** in full doses is also given. **Sparteine** is administered in 2-grain doses for the purpose of supporting the heart and promoting diuresis. For the delirium itself **gelsemine** is given every hour, or every two hours, until its physiological effect is produced; the dose advised is $\frac{1}{25}$ grain. Alcohol is reduced to moderate limits, but is not entirely withdrawn: opium and other narcotics are condemned as not merely dangerous, but useless. Physical restraint is also held to be not permissible. In 450 consecutive cases the results of this line of treatment are described as excellent, and no death from delirium tremens occurred in the whole series. G. E. Pettey (The Hospital, Jan. 15, 1910).

The patient should be carefully fed, **milk** and **concentrated broths** being especially useful. If necessary, **nutrient enemata** are to be administered.

Excellent is hypodermoclysis or the intravenous infusion of **saline solution** in delirium tremens, which increase the amount of the circulating medium in which the toxic materials are dissolved, thereby diluting the poison and bathing the nerve-centers with a more attenuated solution of the same. The amount of circulating fluid is increased above the normal, so that the excretion of fluids through all the eliminatory channels is augmented, thereby carrying off in solution much of the contained toxins. The action of the heart is improved by the filling of the relaxed vessels. These suffice to restore the physiological equilibrium and turn the balance in favor of recovery (Warbasse, Quénu).

[Delirium without hallucinations, and hallucinations alone without any particular delirium are conditions that require special study and care. The physician should not permit such cases to go about without special attendants and watchful care.

Under all circumstances they need the closest watching and are really dangerous, unless guarded, not only to themselves, but others. A delusional alcoholic should be guarded all the time, for the reason that dangerous obsessions may appear any moment. T. D. Crothers.]

ACUTE ALCOHOLIC MANIA (MANIA A POTU).

SYMPTOMS.—The patient, in a wild, ungovernable fury, shouts, stamps, strikes, or kicks, and is, for the moment, uncontrollable. The eyes roll, the face is flushed, and the veins distended and engorged; the muscles are at their highest point of tension, and are in continuous, violent action. The pulse is strong, bounding, and tumultuous. Though mechanically conscious, the subject is filled with "blind fury." He is carried away in a tempest of nervous excitation and passion. The paroxysms of violence sometimes last only a few minutes, at other times for from an hour to several days, with quiet intermissions. Rarely are there delusions, though the infuriated subject may vent his violence on the first animate or inanimate object in his way.

In a few cases the fury is directed against a certain person or thing. Violence is succeeded by calm; a few minutes after a storm the temperature is normal, and during the paroxysm rarely raised. In some constitutions a paroxysm may be provoked by a small quantity of alcohol (Kerr).

DIFFERENTIAL DIAGNOSIS.—It may be differentiated from delirium tremens by the absence of tremors, terror, hallucinations, delusions, the white tongue, nausea, and the delirium of the latter. Further, mania a potu may arise from a small quantity of an intoxicant taken in a short time, while delirium tremens is due to large quantities taken in rapid succession, or from smaller quantities long continued (Kerr).

ETIOLOGY AND PATHOLOGY.—Mania a potu is occasionally seen in chronic inebriates, and most frequently in periodic tipplers. In the latter it often occurs when, after an interval of abstinence, an intoxicant is freely partaken of. Some chronic inebriates invariably suffer acute mania if they drink a single glass of spirits, wine, or beer beyond their usual allowance.

The paroxysms of acute mania resemble those of epilepsy, and a large proportion of police-court drunken offenders are patients of this class. The symptoms are evoked by the pathological action of acute alcoholic intoxication on nervous systems liable to such excitation, either congenitally or from the effects of intemperance, traumatism, or brain-tire. According to Jones, the forms of insanity met with which result from alcoholism are: 1, amnesic; 2, delusional and, 3, chronic varieties which end in dementia.

PROGNOSIS.—The prognosis is much more favorable than in ordinary acute mania, the paroxysm usually rapidly passing away, leaving the patient exhausted and peaceful. Unless alcohol be taken again relapse is rare.

TREATMENT.—But little treatment is generally needed in this condition. Non-alcoholic liquids, such as **milk**, iced milk, milk and soda, or **saline draughts** with **ipecacuanha** and **bromides** are sufficient to bring about recovery. Sometimes **cold affusions** and, in prolonged paroxysms, **wet packs** prove valuable adjuncts.

When violent mania is present, **apomorphine**, ⅛ to ⅙ grain, hypodermically, causes nausea and vomiting and rapid removal of the violent symptoms.

If it persists, **potassium bromide**, in 30-grain doses every two hours, or **morphine**, ¼ grain at long intervals, must be resorted to.

T. D. Crothers,
Hartford.

ALEPPO BOIL. See Oriental Sore.

ALOES (*Aloe*).—The inspissated juice of the leaves of *Aloe vera* or *A. chinensis* (Curaçao or Barbadoes aloes) or of other species, such as *Aloe Perryi* (socotrine aloes, East Africa) and *Aloe spicata* or *A. ferox* (Cape aloes). The plants are indigenous in Africa and India, and are naturalized in the West Indies and along the Mediterranean shores.

PROPERTIES AND CONSTITUENTS.—Curaçao aloes occurs in orange-brown, opaque, and resin-like masses which give off an odor of saffron and have a very bitter and somewhat nauseous taste. Socotrine aloes varies in color from yellowish brown

to dark brown; its odor and taste are similar to those of Barbadoes aloes. Cape aloes is reddish brown or olive-black.

According to A. R. L. Dohme, Curaçao aloes is as efficient as socotrine aloes and less expensive; the greater portion of the latter now sold is made up of the former.

Purified aloes (*aloc purificata*), the form generally employed in medicine, is aloes which has been softened by heating and the addition of alcohol, strained, and dried. It occurs in commerce in pieces or in powder form.

Aloes contains: 1. Aloin, a bitter, crystalline principle present in amounts ranging from 4 to 30 per cent., and composed in socotrine aloes exclusively of barbaloin, to which, in Curaçao aloes, is added the isomeric body isobarbaloin. 2. Emodin (Kraemer), an actively cathartic principle. 3. A yellowish, odoriferous volatile oil. 4. A resinous material, varying according to the species of aloes. 5. Albuminous bodies. 6. Fatty substances. 7. A small amount of gallic acid.

Aloin, official as *Aloinum,* occurs as minute orange-colored crystals or as a microcrystalline powder varying in color from lemon-yellow to yellowish brown. It has little or no odor, is bitter to the taste, and remains unchanged in the air. It is soluble in 65 parts of water and in 10.75 parts of alcohol. Its solutions turn brown on continued exposure, and when alkalies are added present a dark-red color with greenish fluorescence.

DOSE AND PREPARATIONS.—the dose of purified aloes in adults is ½ to 10 grains (0.03 to 0.6 Gm.), the average dose being officially given as 4 grains (0.25 Gm.). The dose of aloin is ½ to 2 grains (0.03 to 0.12 Gm.). Average dose: 1 grain (0.065 Gm.). The other official preparations of aloes are:—

Tinctura Aloes (10 per cent.), containing also 20 per cent. of licorice. Dose: ¼ to 1 fluidram (1 to 4 c.c.). Average dose: 30 minims (2 c.c.).

Tinctura Aloes et Myrrhæ, containing aloes, myrrh, and licorice, of each, 10 per cent. Average dose: 30 minims (2 c.c.).

Extractum Aloes.—A watery extract, dried and powdered. Dose: ½ to 6 grains (0.03 to 0.4 Gm.). Average dose: 2 grains (0.125 Gm.).

Pilula Aloes, containing aloes and soap, of each, 2 grains (0.13 Gm.). Dose: 1 to 4 pills.

Pilula Aloes et Ferri, containing purified aloes, dried ferrous sulphate, confection of rose, and aromatic powder, of each, 1 grain (0.07 Gm.). Dose: 1 to 4 pills.

Pilula Aloes et Mastiches (Lady Webster's Dinner Pill), containing purified aloes, 2 grains (0.13 Gm.); mastic, ⅔ grain (0.04 Gm.), and powdered red rose, ½ grain (0.03 Gm.). Dose: 1 to 4 pills.

Pilula Aloes et Myrrhæ, containing purified aloes, 2 grains (0.13 Gm.); myrrh, 1 grain (0.07 Gm.), and aromatic powder, ⅔ grain (0.04 Gm.). Dose: 1 to 4 pills.

Aloes is also a constituent of the following:—

Tinctura Benzoini Composita, containing benzoin, 10 parts; aloes, 2; storax, 8; tolu, 4. Dose: 30 minims (2 c.c.).

Extractum Colocynthidis Compositum, containing extract of colocynth, 16 parts; purified aloes, 50; resin of scammony and powdered soap, of each, 14; cardamom, 6. Dose: 7½ grains (0.5 Gm.).

Pilula cathartica composita.

℞ *Ext. colocynthidis comp.* ..... gr. i⅓ (0.08 Gm.).
Hydrarg. chloridi mitis ..... gr. j (0.06 Gm.).
Resinæ jalapæ .. gr. ⅓ (0.02 Gm.).
Cambogiæ pulveris ..... gr. ¼ (0.015 Gm.).

Dose: 2 pills.

Pilula cathartica vegetabilis.

℞ *Ext. colocynthidis comp.* ..... gr. j (0.06 Gm.).
Ext. hyoscyami . gr. ss (0.03 Gm.).
Resinæ jalapæ .. gr. ⅓ (0.02 Gm.).
Ext. leptandræ, Resinæ podophylli .....āā gr. ¼ (0.015 Gm.).
Olei menthæ piperitæ ..... gr. ⅛ (0.008 Gm.).

Dose: 2 pills.

Pilula rhei composita.

℞ *Rhei pulveris* ... gr. ij (0.13 Gm.).
Aloes ..... gr. iss (0.10 Gm.).
Myrrhæ ..... gr. j (0.06 Gm.).
Olei menthæ pip.. gr. 1/12 (0.005 Gm.).

Dose: 2 pills.

Pilula laxativa composita.

℞ *Aloini* ..... gr. ⅕ (0.013 Gm.).
Strychninæ ..... gr. 1/128 (0.0005 Gm.).
Ext. belladonnæ fol. ..... gr. ⅛ (0.008 Gm.).
Ipecacuanhæ pulv. gr. 1/16 (0.004 Gm.).
Glycyrrhizæ pulv. gr. ¾ (0.046 Gm.).

MODES OF ADMINISTRATION.—Aloes is entirely soluble in 5 parts of alcohol, but only partly soluble in water. It is generally administered in pill form on account of its strongly bitter taste. It acts slowly, and can, therefore, be administered at bedtime with the expectation that its effects will be exerted the next morning. Aloes may be used alone, but is oftener given in conjunction with other cathartic remedies and correctives, as in several of the preparations above mentioned. Certain agents have been found to increase its effects, including bile, iron, and the alkalies. Equal parts of purified aloes and dried oxgall may be administered in a salol-coated pill with advantage. Aloin, while somewhat less certain in its action than aloes, is often considered preferable because of the smaller dose required and less liability to cause "griping." It is frequently employed in the aloin, belladonna, and strychnine pills, of which the official form (*Pilula Laxativa Comp.*) has already been referred to.

INCOMPATIBLES.—Aloes is incompatible with mineral acids, iodine, silver nitrate, tannic acid, phenol, menthol, thymol, and salicylic acid.

CONTRAINDICATIONS.—It is generally inadvisable to prescribe aloes in cases of hemorrhoids, owing to its effect of causing congestion of the pelvic organs; in cases accompanied by free secretion of mucus in the bowel, however, it may, on the contrary, prove beneficial. Aloes is likewise contraindicated in pregnancy and in menorrhagia occurring in plethoric women. In view of its elimination, in part, through the milk, it is not available for use as a purgative in nursing women.

PHYSIOLOGICAL ACTION.—In small doses aloes and aloin exert a *stomachic* effect. The secretions of the alimentary tract are augmented. With larger doses (2 to 4 grains) its well-known *laxative* effect is obtained, ten to fifteen hours usually elapsing from the moment of extubation until the first evacuation results. The effect is due to stimulation of the muscular coat as well as the glands of the large intestine, and is generally attended with a certain amount of griping pain. Through its property of inducing hyperemia in the ovaries and uterus, aloes also has distinct value as an *emmenagogue*.

Though easily absorbed through abrasions and ulcerated areas (exercising thereafter its characteristic laxative and other effects), aloes exerts no local therapeutic action. It is eliminated with the feces, slightly with the urine, and,

in nursing women, with the mammary secretion.

Aloin, the so-called active principle of aloes, is believed not to exert its effect in the bowel until it has undergone certain changes in composition. The resulting active compound, which can be made from the pure, crystalline aloin by boiling a solution of the latter (Cushny), is probably contained in the crude drug after the crystalline aloin has been extracted. Hence, the fact that in practice crude aloes is found to act with greater certainty and speed than the principle aloin. It has been found that in human beings placed upon an exclusive meat diet aloin acts much more strongly than in persons subsisting on a mixed diet. The aloin is believed to be altered through processes of hydrolysis and oxidation into *emodin* (oxymethylanthraquinone), an active constituent of many other drugs of this class, such as senna, cascara sagrada, and rhubarb, which induces the purgative effect. Injected under the skin or into a vein, aloin for the most part passes into the bowel, there exerting an irritant effect and inducing purgation. In the rabbit, however, in which aloin is excreted to a large extent through the kidneys, pronounced irritation of these organs is produced, catharsis being, on the other hand, an infrequent result. A nephritis is generally induced, in which the epithelium of the tubules is particularly involved, the glomeruli being largely spared. The urine contains casts, blood, proteids, and leucocytes; it may be either augmented or decreased in quantity (Mürset).

UNTOWARD EFFECTS.—The use of aloes over long periods is said to favor the production of hemorrhoids. Large doses of aloes induce burning at the anus; sometimes blood-stained stools, painful micturition, and uterine discomfort. Dosage exceeding 0.20 Gm. (3 grains) per diem, when persisted in for any length of time, leads inevitably to intestinal irritation and congestion.

According to Pouchet, massive single doses of aloes may induce general prostration with slowing of the pulse and a fall in the temperature.

THERAPEUTIC USES.—As a Laxative.—Aloes is most frequently used in the treatment of **constipation** due to intestinal atony. In moderate doses it stimulates the intestinal mucosa to increased secretory activity, thereby facilitating the discharge of the bowel contents. Its continued use is, however, to be avoided, since on prolonged administration a tendency to aggravation of the disorder present is likely to appear.

A characteristic feature of the action of aloes is the congestion it tends to produce in the intestinal tract (especially the rectum) and pelvic organs. This property has led to its occasional use as a derivative in conditions associated with cerebral or pulmonary congestion, blood being thereby removed from the engorged area. Experimental work has shown that aloes, in common with other purgatives of the anthracene series, does not act as a true cholagogue, *i.e.,* does not increase the amount and concentration of the biliary secretion. It does, however, by accelerating peristalsis, promote the removal of bile from the intestinal tract, and prevent its reabsorption from the duodenum into the liver. For the relief of **hepatic congestion,** Rendu has recommended the use of aloes in combination with calomel and gamboge. The cathartic effect of aloes has been found to be

greatly favored by the presence of bile, which is believed to assist by exerting a solvent action on the drug, thereby hastening its effect. In view of this observation, too, it is thought that in cases of obstructive jaundice the action of aloes is interfered with owing to the deficiency of bile.

Alkalies and iron assist the purgative action of aloes. The former facilitate the decomposition of aloin, whereby a more strongly irritant and cathartic substance is formed. Iron similarly favors the oxidation of aloin. In **chlorosis** the aloes and iron combination is often employed, as in the official pill of aloes and iron. It is best, however, not to use this pill, owing to the particularly marked constipating effect of the preparation of iron it contains. The pyrophosphate of iron or dialyzed iron is to be preferred. Nux vomica and belladonna, or their active alkaloids, are also frequently combined with aloes, the former to improve the tone of the intestinal muscles, and the latter to prevent "griping." The last-named effect can also be minimized by giving the drug after meals.

Robin recommends the following pill as a mild, but efficient laxative:—

℞ *Aloes,*
Ext. of liquorice ..āā 1 gr. (0.06 Gm.).
Gamboge ..... ½ gr. (0.03 Gm.).
Ext. of belladonna,
*Ext. of hyoscyamus,*āā 1 gr. (0.06 Gm.).
Enough for 1 pill. Take one or two on retiring.

Aloin possesses over crude aloes the advantages of smaller bulk and less tendency to cause intestinal irritation, but these are partly offset by the diminished certainty and celerity of its action.

In large doses aloes acts as a drastic, inducing first eructations and a feeling of weight in the stomach, then copious stools with colicky pains. Its use as such, however, is to be avoided, because of the marked intestinal irritation and congestion it causes.

As a Stomachic.—In doses not exceeding 1 to 1½ grains (0.06 to 0.10 Gm.) daily, aloes improves the appetite and stimulates the gastric functions.

As an Emmenagogue.—In anemic women with **amenorrhea** aloes is sometimes given to favor the menstrual flow. It is best given four days before the expected period, and its action is greatly enhanced by combination with iron. In amenorrhea due to other causes the official pill of aloes and myrrh may be tried, the congestive influence of the active drug tending to facilitate menstruation; good results, however, are to be expected less frequently than in the anemic cases.

In Hemorrhoids.—Though the use of aloes as a laxative is contraindicated in the presence of hemorrhoids, this drug, given in small doses, has been claimed by some to be beneficial in cases where the circulation in the inferior hemorrhoidal veins is particularly sluggish and the pile masses protrude, inducing tenesmus. The use of aloes in very small doses when hemorrhoids are associated with irritation and frequent small, thin evacuations has been advocated by Fordyce Barker.

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ALOPECIA.—Baldness; calvities.

DEFINITION.—Alopecia is a physiological or pathological deficiency or loss of hair, either partial or complete. The forms of alopecia may be classified as follows:—

I. Congenital alopecia.
II. Senile alopecia.
III. Premature alopecia.

- (*a*) Idiopathic.
  - Hereditary predisposition.
    - Seborrhea.
    - Eczema seborrhoicum.
    - Psoriasis.
    - Erysipelas.
    - Lupus erythematosus.
    - Syphilodermata.
    - Folliculitis.
    - Tinea tonsurans.
    - Tinea favosa, etc.
- (*b*) Symptomatic.
  - (1) Local diseases.
  - (2) General diseases.
    - Acute
      - Typhoid fever.
      - Variola.
      - Scarlatina.
      - Pregnancy.
    - Chronic
      - Syphilis.
      - Leprosy.
      - Myxedema.
      - Neurasthenia.
      - Chronic intoxications.
      - Anemia.
      - Diabetes.
      - Cancer.
      - Uric acid diathesis.
      - Phthisis, etc.

Congenital Alopecia.—This commonly manifests itself either as a scanty growth, a development only in certain localities, or as a retarded appearance of the hair. In rare cases there may be complete absence of the hair due to arrested development of the follicles. In such cases hereditary predisposition is usually present, and there are apt to be, in addition, delayed or defective dentition, and at times developmental defects of the nails.

[J. H. Hill (Brit. Med. Jour., vol. i, 1881, page 177) has described a race of hairless Australian aborigines. Jay F. Schamberg.]

> "Alopecia congenita familiaris," a congenital absence of hair occurring in several members of a family, observed in a brother and sister, aged respectively 1½ and 3½ years. They were both born with hair on the scalp, but this began to fall out in a few weeks, till the scalps became perfectly bald. When examined the scalps were smooth, atrophic, and glossy. Inflammatory changes were absent. In both the lanugo hair was absent in the breast and extremities, and the eyelashes were deficient. The nails were not affected in either case. The mother gave a history of another boy in the family whose hair had come out at four weeks, and a fourth case was also mentioned.
>
> Histological examination of the first 2 cases showed the remains of the original lanugo hairs in the forms of shrunken hair follicles, in which the papillæ were absent and the inner root-sheaths, as well as the hairs, had disappeared. In some cases the follicles had become transformed into cysts connected with the sebaceous glands. The parents were healthy and had normal hair. Personal conclusion that the condition is the result of an interference with the normal hair change which should begin in utero. The lanugo follicles had undergone regressive changes, and no permanent hairs

had developed. Kraus (Archiv f. Derm. u. Syph., Aug., 1903).

Congenital alopecia may be divided into three classes: 1. Complete and universal absence of hair at birth, not succeeded later in life by a piliary growth. This is believed to be an intrauterine atrichia due to a failure of development of the hair-pouches. 2. Universal congenital hypotrichiasis, in which at birth hairs exist in all regions of the body, but later fail to be succeeded by filaments normal in length, vigor, color, and texture. Two subvarieties of this condition have been recognized: (*a*) the infant at birth is provided with the relatively long hair of most normal infants; this in due time fails and is replaced by a scanty down, which later in life fails to insure a normal hirsuteness of the scalp; (*b*) after birth the infant fails to lose the temporary hair of the scalp, which persists, but later develops merely a scanty or ill-developed piliary growth. 3. Complete or partial absence of hair at birth in definitely circumscribed regions, such as the scalp, the brows, the pubes, or the axillæ. The anomaly is rare, and persistence through life still rarer. Many published observations are lacking in detail of special importance. Nevins Hyde (Jour. of Cutan. Dis., Jan., 1909).

Senile Alopecia.—As the name indicates, this form of baldness is observed in the aged. With the atrophic skin changes that accompany senility there takes place a gradual thinning of the hair, beginning upon the vertex of the scalp, the frontal and the temporal regions, and slowly leading to a more or less complete baldness of the calvarium. Under the microscope the cutis proper and the hypoderm exhibit thinning and atrophy.

Case of periodical shedding of the hair in a woman aged 21 years. Her hair was shed every winter and grew in again in the summer. Last winter she became entirely bald, and this summer her hair did not grow in again. Absence of hair existed on the general surface, which began in circular patches when she was 12 years old. H. Ledermann (Jour. of Cut. Dis., Jan., 1904).

Premature Alopecia.—This form of alopecia is encountered chiefly in individuals between the ages of 20 and 35. G. T. Elliott found that among 344 private cases of premature alopecia, 64 per cent. occurred under the age of 30. Premature alopecia may be either *idiopathic* or *symptomatic*.

In the *idiopathic* variety the scalp presents no abnormal condition. At first only a few hairs fall out from time to time, being replaced by a shorter or finer growth. Later these fall and are followed by still finer hairs. In this manner the greater part of the hair of the scalp may be gradually lost. The affection occurs in both sexes, although much less frequently and less completely in women than in men. Heredity appears to be a strong predisposing factor.

There is a growing opinion that the so-called idiopathic baldness is exceptional, and that most cases of premature alopecia are associated with seborrhea in some form. Of 344 private cases of premature alopecia studied by Elliott, 316 had seborrhea. Jackson found 75 per cent. of 300 cases due to seborrhea.

The *symptomatic* form results from various local and general diseases. Rapid falling of the hair (defluvium capillorum) commonly follows acute diseases, such as typhoid fever, smallpox, etc. Full regeneration of the hair follows the restoration to health. Rapid and extensive loss of hair occurs with frequency in the early stages of syphilis. The hair is also thinned or lost in such cachectic conditions as phthisis, myxedema, diabetes mellitus, leprosy, etc.

Areas of absolute alopecia which occur in the scalp or beard in syphilis may be small and few, well circumscribed, lasting a short time, but recurring often. This is very different from the general thinning of the hair seen early in the disease, which never returns. A. Fournier (Jour. des Praticiens, Jan. 19, 1901).

Alopecia is not a common or regular symptom of the early stages of syphilis. The slight loss of hair which is constantly taking place in healthy individuals as the result of the physiological change in the hair continues its existence through and beyond the course of syphilis, and must be taken into consideration before attributing to syphilis a loss of hair so slight as to pass unnoted or scarcely attract the patient's attention. Klotz (Jour. of Cut. Dis., Mar., 1907).

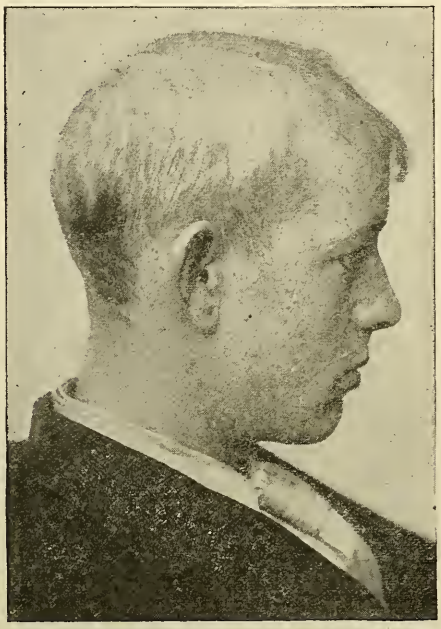
Alopecia Seborrhœica. — Considerable difference of opinion exists as to what constitutes the seborrheic process; the comprehension of the relation of seborrhea to baldness is thereby embarrassed. Nearly all writers are agreed that *dandruff* has not the same significance for all observers. Sabouraud holds that dry pityriasis of the scalp is not a depilating affection itself, but that it is frequently associated with the true seborrhea. Many clinicians speak of an *alopecia pityrodes* in which there is either a seborrhea with fatty crusts or a pityriasis with abundant scaling. Crocker does not restrict alopecia seborrhœica to the oily form: according to his experience there is either "an excessive greasiness of the surface from oily seborrhea, or fine, glistening, powdery scales, or greasy scales lying closely on the scalp and requiring to be scraped off, or yellowish, fatty matter looking like pale-yellow wax."

New clinical form of atrophic alopecia, for which the term "pseudopelade" is adopted. It is a process of atrophy and sclerosis affecting the hair-covered regions of the body, especially the scalp, terminating in patches of baldness, smooth, of pseudocicatricial aspect. It seems to be closely allied to erythematous lupus and keratosis pilaris. Brocq, Lenglet, and Ayrignac (Annales de dermat., vol. i, No. 3, 1905).

Analysis of 679 cases of loss of hair, chiefly alopecia simplex and alopecia furfuracea. There were, however, 86 cases of alopecia and lesser numbers due to ringworm and syphilis, and 2 cases from X-rays. Women seemed to be more affected by loss of hair, in the relative proportion of 54 to 46, but possibly they consult physicians more freely on this account than do men. The author finds that heredity, dandruff, systemic depression, fever, operations and maltreatment of the scalp have been connected in the patients' minds with the fall of hair and, according to his figures, hereditary taint exists in 30 per cent. while dandruff was present in 443 patients, a percentage of more than 79. Systemic depression was recorded in 120 cases, fever in 63, and maltreatment was evident in 277 cases, or nearly half of the whole number. Most patients were unable to remember the date of beginning alopecia, but it seems, with all the accurate data that could be obtained, that in the clinically uncomplicated loss of hair, it began before 30 in 84 per cent. of the males. In females it appeared at this early age in a much less percentage and seemed to be of later development. Dandruff appeared also earlier in men than in women, being about twice as frequent between the ages of 16 and 25. C. J. White (Jour. Amer. Med. Assoc., Sept. 24, 1910).

ETIOLOGY AND PATHOLOGY. —Dandruff is generally regarded as the most potent cause of baldness. It is a plausible and attractive theory to attribute the process to microbic invasion. Sabouraud has brought forth strong evidence to show that his microbacillus is intimately associated with, if not the cause of, oily

seborrhea. He likewise regards this organism as the cause of baldness. The microbacillus, according to him, enters the mouth of the hair follicle, multiplies, and forms a thin microbic lamina, which separates the hair shaft from the follicular wall. Epithelial irritation causes the encysting of the bacilli in a plug or cocoon. Then



Alopecia from a cured tinea favosa. (*Schamberg.*)

follows increased sebaceous flow, hypertrophy of the sebaceous gland, and progressive atrophy of the hair papillæ. Sabouraud recognizes other causes which render the soil favorable, such as city life, insufficient exercise, excessive meat diet, gout, heredity, etc. If baldness has a microbic origin, Sabouraud is certainly correct in regarding the above causes—causes which are operative in the busy life of great cities—as of vast importance. Premature baldness is rare or absent among savages and is less common in country than in city districts.

Many other factors have been invoked as causes of baldness, such as the too frequent wetting of the hair, the wearing of stiff hats which constrict the temporal arteries, etc. It is also stated that brain workers are particularly subject to premature alopecia; this is probably more the result of sedentary life than of intellectual activity.

> The skin of the scalp overlying the epicranial aponeurosis has no underlying muscles to exercise it, and has only the action of the occipitofrontalis to depend on, and moves only when that muscle is put into action. That is not often. The scalp is very vascular; there is nothing to interfere with or retard the arterial supply, but there is also nothing to accelerate the return flow—no active muscular exercise in the part whatever to hurry along the waste products and the deoxygenized blood in the vessels. These structures being superficial and easily compressible, their compression by the rim of the hat will further retard the flow. In women the scalp is well exercised by the combing, plaiting, and throwing from side to side of the hair—men scarcely give more than a moment to the brushing and combing of their hair. Massage is the treatment to be applied, especially as a preventive. George Elliott (Dominion Med. Monthly, Mar., 1902).

Alopecia areata is often caused by traumatisms of the head. The existence of anatomical and functional lesions of the central nervous system must be admitted, the state of central irritation giving rise to peripheral trophic disturbances, which manifest themselves by the appearance of hyperalgesic zones. Possibly, vascular lesions analogous with arteriosclerosis are the cause of the falling out of the hair. At any rate, the nervous lesion is the predominant etiological factor. Psychic traumatism, especially fright, has an identical effect. Weichselmann (Deut. med. Woch., Nov. 12, 1908).

Alopecia of dental origin often follows a painful attack of trigeminal

neuralgia caused by the teeth (18 out of 25 cases). This attack may precede the depilation by two or three months, but more commonly it occurs in the preceding month. It occurs on the same side as the trigeminal attack, more frequently on the left side because dental lesions are more common on the left side. It appears by preference in certain predisposed zones, as if there was a relation between the seat of the dental irritation and the seat of the initial area of alopecia. Thus, in 16 cases of trouble with the lower wisdom tooth the author found alopecia localized on the same side of the nucha in 14. It follows alveolar and gingival irritation rather than dental irritation proper. Thus, in 25 cases of dental alopecia the author traced the cause in 3 cases to inflammation of the dental pulp, in the remaining 22 to troubles outside the teeth. These irritations seem to act differently upon the trigeminus. It is accompanied by certain phenomena, such as hyperesthesia, erythrosis, hyperthermia, adenopathy, lymphangeitis, and edema, grouped by Jacquet under the name of the dental syndrome. The areas are generally small in size and few in number. The prognosis is good. The cure is rapid and often immediate after dental intervention alone. Rousseau-Decelle (Presse méd., Feb. 6, 1909).

PROGNOSIS. — Alopecia seborrhœica gradually progresses, unless checked by treatment, to a denudation of the vertex leaving a fringe of hair in the temporal and occipital regions. Appropriate treatment, particularly if instituted early, will sometimes check the hair loss and lead perhaps to some regrowth. If systemic conditions are present which render the scalp a favorable nidus, the outlook is more unfavorable.

TREATMENT. — The treatment must be directed toward the existing seborrheic process. The measures employed relate both to general and local treatment. **Outdoor life, exposure of the scalp to sunlight, the restricted use of meats** (Sabouraud says baldness is less common in vegetarians), the avoidance of excesses of all kinds, are to be recommended.

Such tonics as **iron, strychnine, phosphorus, arsenic, and codliver oil** may occasionally be prescribed with advantage.

Local treatment is of great importance, particularly when dandruff is present. It consists of the proper cleansing of the scalp and the stimulation of the sebaceous glands to healthy action.

The **tincture of green soap** makes an admirable shampoo for the removal of epithelial and sebaceous *débris*. This may be advantageously followed by such a hair-wash as:—

℞ *Resorcinolis* .... ʒij (8 Gm.).
Acidi acetici ... fʒj-fʒij (4-8 c.c.).
Ol. ricini ..... fʒss-fʒj (2-4 c.c.).
Alcoholis, q. s. ad fʒvj (180 c.c.).
Ol. bergamott... ♏xl (2.4 c.c.).

When greater stimulation is desired, the following lotion may be used:—

℞ *Hydrarg. chlor. corros.* ..... gr. viij (0.5 Gm.).
Betanaphtholis . gr. xxv (1.6 Gm.).
Glycerini ..... fʒj (4 c.c.).
Alcoholis ..... fʒiv (120 c.c.).
Aquæ cologniensis ..... fʒss (15 c.c.).
Aquæ ..... fʒiiss (75 c.c.).
Sig.: Hair-wash; part the hair and apply with a small sponge.

Another lotion frequently prescribed where stimulation is desired is as follows:—

℞ *Tinct. cantharidis* ..... fʒvj (24 c.c.).
Tinct. capsici,
Olei ricini ....āā ♏xxx-fʒj (2-4 c.c.).
Spts. myrciæ (*bay rum*), q. s. ad fʒvj (180 c.c.).

It is a good plan in many cases to use an ointment in conjunction with hair lotions. The lotion may be used each

day, and the pomade applied once or twice a week. The latter should be rubbed in in very small quantities, so as to avoid disagreeable greasing of the hair. When ointments are used conjointly with washes, the glycerin or oil in the lotion may sometimes be advantageously omitted. Sulphur is the most useful agent for scalp pomades when any seborrhea is present. The following ointment gives most satisfactory results:—

℞ *Sulph. præcip.* ..... ʒj (4 Gm.).
Adipis ..... ʒj (31 Gm.).
Ol. bergamott ..... ♏xl (2.4 c.c.).

Daily digital **massage** of the scalp is distinctly useful, as is also the **vigorous use of the hairbrush** to produce hyperemia of the scalp.

Successful treatment depends upon the promptness with which one first notices that the hair is beginning to fall. Healthy hairs do not come out, and if hairs are found on the pillow, on the clothing, or in the hairbrush, the indication is given for beginning the treatment. One of the most important, yet very generally neglected, prophylactic measures consists in **frequent ablution of the head,** a measure that is still considered injurious by many people. On the contrary, frequent shampooing and rubbing of the head is the best preventive of baldness. Another feature on which the author lays much stress is the necessity for cleanliness in all utensils used in the barber shop or in private.

Actual baldness cannot be cured, but a great deal can be done to prevent its onset by properly treating the tendency to falling of the hair. A course of treatment is outlined, of which the following are the most important features: **Daily shampooing** with soap and hot water, followed by drying and the application of a 1:1000 solution of **bichloride of mercury.** This is allowed to evaporate, and the scalp is then rubbed with a 1:400 solution of **thymol or naphthol in alcohol.** Finally, an ointment is applied containing 1 part of **salicylic acid,** 2 of **tincture of benzoin,** and 50 of **vaselin.** In obstinate cases the treatment is begun by the application of **tar liniment,** which is removed ten minutes later with the soap. Lassar (Deut. med. Woch., July 5, 1906).

The most satisfactory lubricant is **cocoanut oil.** It keeps the hair soft and silky and does not mat the hair or plaster it down. A good **shampoo** about once a month suffices. The **wire brush** keeps the scalp pretty free from dirt and dandruff. By its gentle and not disagreeable friction of the scalp, it promotes the circulation and thus brings nourishment to the hair-bulbs, and gives vigor to the growing hair. S. Hendrickson (Jour. Amer. Med. Assoc., Sept. 2, 1911).

The frequency with which the scalp should be washed depends entirely upon the degree of oiliness of the scalp and hair. A greasy scalp requires more frequent cleansing than a dry one. In a general way it may be said that the scalp should be washed about once in two or three weeks. If the skin is very dry afterward, a pomade should be employed. **Soaps** containing **sulphur** and **tar** are useful. Some of the German superfatted soaps, especially one containing **sulphur, salicylic acid,** and **resorcin,** are particularly eligible for the purpose.

Several cases of very severe alopecia in which the employment of **static electricity** had given the best results. In 4 cases this mode of treatment was successful; in 1 unsuccessful. The successful cases were all cured, and this after about twenty or thirty sittings. The patients were submitted to the electric bath, and sparks were discharged on the smooth, hairless patches. R. Pivani and J. Blasi (Annali di Elet. Medica e Terapia, Apr., 1902).

The **high-frequency spark** employed in a lady, aged 30 years, who had some early osteoarthritic changes in the small

joints of the hand and came to the writer complaining of slight seborrheic rash on the face and considerable thinning and falling of hair. The results were brilliant. A thick growth of hair of good quality ensued, but the same application failed afterward in apparently similar conditions. David Walsh (Lancet, June 15, 1907).

The drugs most successful in treating loss of hair are **euresol, bichloride of mercury, captol** and **chloral hydrate.** The final results of treatment are almost disheartening, but from a temporary point of view we may expect good or very good response in 48 per cent. of men and in 56 per cent. of women. C. J. White (Jour. Amer. Med. Assoc., Sept. 24, 1910).

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ALOPECIA AREATA.—Alopecia circumscripta; area celsi.

DEFINITION.—Alopecia areata is a disease of the hairy system characterized by the more or less sudden occurrence of round or oval circumscribed bald patches, in rare cases coalescing and producing total baldness.

SYMPTOMS.—The disease is usually limited to the scalp. The patches are circumscribed and round, and vary in size from a coin to the palm of the hand. The skin is smooth, soft, of a dead-white color, and totally devoid of hair. Occasionally the patches are pinkish as a result of slight hyperemia. The follicular openings are contracted and less prominent than in the healthy scalp.

To the feel the skin is thin, soft, and pliable. In the beginning, the patches are level or slightly elevated, while later they are sometimes slightly depressed.

The course of the disease is extremely variable. In some cases the bald patches develop suddenly in the course of a few hours. In other cases, the hair loss is gradual, extending over a period of a few days or weeks. The areas then spread by peripheral extension until they reach a certain size, when they remain stationary.

Alopecia totalis following an ordinary alopecia areata. (*Schamberg.*)

In some cases the entire scalp becomes denuded of hair, giving to the patient a most grotesque appearance. In extensive cases it is by no means rare for the eyebrows and eyelashes to be lost. In men the bearded region of the face may be involved, either alone or in conjunction with the scalp.

The duration of the disease varies greatly. Recovery seldom occurs in less than a few months, while many cases last several years. The disease

may occur at any period of life. In young individuals the hair usually returns sooner or later. In adults, the baldness may persist and prove refractory to all treatment.

When regrowth occurs, the patch is first covered by fine, downy, whitish hairs which are either shed or later converted into coarse and pigmented

Alopecia areata. (*Schamberg.*)

hairs. Not infrequently the hair grows in and the patient thinks he is on the road to recovery, only to have his hopes shattered by the hair falling out again. As a rule, there are no subjective symptoms.

Alopecia areata occurs with similar frequency in the two sexes. It is more common in youth and early adult life than in other age periods. Crocker states that, of 506 hospital cases, 214 were under 15 years of age, and 214 occurred in persons between the age of 15 and 35.

Case in a well-developed girl, 4 years of age, whose general health had always been good. She is said to have had fairly thick blond hair until two years ago, when small bald patches began to appear. These rapidly increased in size, and soon the case became one of the so-called malignant type. At present practically all of the scalp hair has been lost, as well as the eyebrows and lashes. Kingsbury (Jour. of Cutan. Dis., July, 1909).

ETIOLOGY.—They are two distinct theories of the causation of alopecia areata. One school insists that the disease is parasitic, and cites occurrences of epidemics in institutions as proof of this view. Epidemics have been observed chiefly in France and Germany: Bowen and Putnam describe an outbreak in an institution in this country.

The bacteriological theory of alopecia areata still requires confirmation, none of the organisms at present found having justified a claim to be regarded as the specific cause. On the other hand there is evidence of contagiosity and infectiousness. As regards the frequency of the affection, it would appear that this is on the increase. Caution must, however, be used in assuming this increase to be actual. The greater frequency with which people now consult specialists, and the consequently greater accuracy of diagnosis, may give rise to fallacies in this direction. It represents 1.4 per cent. of all cases treated by the writer. The chief age incidence lies between 20 and 30, and the sexes are affected in the proportion of about 7 males to 3 females. O. Lassar (Dermat. Zeit., Sept., 1900).

Among 30 cases observed within a brief period by the writer, there were no instances in which contagion could be traced. He does not think that the existence of this disease in epidemic form has been proved, notwithstanding that instances in which it occurs in barracks are well known. This fact may be explained in other ways. M. Cruyl (La Clinique, Apr. 27, 1901).

The cause of alopecia areata is not an infection, but some neurotrophic influence. Division of the second cranial nerve experimentally causes it; besides, thallium acetate applications cause neurotrophic affections of the entire body. And with atrophy of the fibers of the sympathetic nerves in certain regions alopecia results, especially when the trigeminus is affected. From his observations the writer believes alopecia areata always to be neurotrophic in character. E. Richter (Berl. klin. Woch., Dec. 29, 1902).

Giovanni observed that patients to whom he was administering acetate of thallium became affected with alopecia. The writer studied the effect of small doses of this drug on mice, given in food. The result of its administration was that the hair came out on different parts of the body. This effect was not due to any appreciable local action of the drug on the skin, but in the writer's opinion to certain disturbances affecting the peripheral nervous system of a trophic nature. Buschke (Berl. klin. Woch., Nu. 53, 1900).

Alopecia areata is trophoneurotic in origin, as first urged by Jacquet, who noted some close relation between alopecia and dental neuralgia. His investigations show that neuralgia occurs before, with, or after the alopecia, in almost all cases. This dental theory of the origin of alopecia is confirmed by a case-history which the writer quotes, a child in whom the condition disappeared after the affected gum had been cauterized. F. Trémolières (Presse méd., June 14, 1902).

Case of alopecia areata affecting man and wife. In the man alopecia, vitiligo, and blanching of the hair and beard occurred almost at the same time after emotional trouble in a patient of a neuroarthritic diathesis. The wife, also a neuroarthritic subject, suffered from the same emotional cause, and had loss of hair and eyebrows. In these cases the cause appears to be trophoneurotic. In the male the patches were typical of alopecia areata; in the female, irregular and disseminated. Lévy (Jour. des mal. cut. et syph., May, 1902).

Recalling Jacquet's theory that baldness is of nervous origin, and is connected with skin diseases, dental troubles, and crises of gastrointestinal and other origin, the writer refers to a case in which the cure of a fistula in ano, complicated with entire loss of hair, was succeeded by complete restoration of eyelids, eyebrows, and hair of the scalp. Eyraud (Presse méd., Mar. 30, 1904).

On the other hand, there is irrefutable clinical evidence of the neuropathic origin of cases of alopecia areata. Nervous shock, such as fright, prolonged anxiety, etc., and traumatism to the scalp have been directly followed by areate loss of hair.

[I recently saw a boy admitted to the Polyclinic Hospital for the fracture of the skull who developed alopecia areata before leaving the institution. Max Joseph has produced the disease in cats by excision of the second cervical ganglion. J. F. S.]

It would, therefore, appear that there are two varieties of alopecia areata, the one parasitic and the other trophoneurotic. In the epidemic observed by Bowen and Putnam, the patches were not identical with those commonly observed, but were smaller and more irregular in shape. Some of the English dermatologists are of the opinion that alopecia areata is prone to occur in those who have at some previous period suffered from ringworm of the scalp. Sabouraud regards his microbacillus as the probable cause of alopecia areata, though the influence of syphilis is not overlooked by him.

Extensive alopecia due to syphilis, either acquired or hereditary, oftener than to any other single cause, as suggested by the success obtained with antisyphilitic remedies. Sabouraud (Ann. de derm. et de syph., p. 545, 1910).

Study of 14 typical cases of alopecia areata. In 11 of these the writer obtained a positive Wassermann reaction, when there were no symptoms of syphilis, either hereditary or acquired. The 3 negative cases were the subjects of single alopecic patches which were speedily cured by local stimulation. Du Bois (Ann. de derm. et de syph., Nov., 1910).

PATHOLOGY. — Both Giovanni and Robinson found evidences of inflammatory disturbances, chiefly in subpapillary layer. Perivascular cell infiltration was observed in both early and late lesions. Subsequently atrophic changes take place with destruction of the hair papillæ.

The characteristic hair of alopecia areata has the shape of an exclamation point. The upper part is pigmented and normal, while the lower portion is atrophied and without pigment. Sabouraud describes an ampullar swelling (*the peladic utricle*) filled with the microbacillus in the upper third of the hair follicle.

Alopecia Areata.	Ringworm.
1. Rapid onset.	1. Slow, insidious onset.
2. Patches are:—	2. Patches are:—
(*a*) Totally devoid of hair.	(*a*) Covered with broken-off stumps.
(*b*) Pale or whitish in color.	(*b*) More or less reddened.
(*c*) Smooth or soft.	(*c*) Rough and scaly.
(*d*) Follicles contracted.	(*d*) Follicles prominent; "goose-flesh" appearance.
3. Absence of fungus.	3. Trichophyton fungus present.
4. Common in adolescence and adult life.	4. Occurs almost exclusively in childhood.

The baldness of early syphilis may bear some resemblance to alopecia areata. Apart from the presence of other evidences of the disease, the patches are moth-eaten in appearance and not sharply circumscribed. The surrounding hair and scalp are lusterless and dirty, whereas in alopecia areata they are perfectly normal.

PROGNOSIS.—In children recovery usually takes place. In young adults the prognosis is usually favorable, while in advanced adults it is unfavorable. The longer the disease has persisted, the more unfavorable is the prognosis. The duration of the disease is uncertain and relapses are not uncommon.

TREATMENT.—The internal treatment consists of the use of such tonics as **iron, strychnine, quinine, codliver oil, phosphorus,** and **arsenic.** Duhring considers arsenic to be "especially serviceable."

The local treatment has for its purpose the stimulation and rubefaction of the scalp with the object of increasing the blood-supply to the follicles. Many cases terminate in spontaneous recovery, and conservative judgment is desirable in interpreting the value of remedies employed. Among the many medicaments which have been advised are **alcohol, cantharides, capsicum,** the **essential oils, turpentine, carbolic acid, trikresol, ammonia, sulphur, iodine, mercury, chrysarobin, betanaphthol,** etc.

The following lotion will be found of value:—

℞ *Tinct. cantharides,*
Tinct. capsici, of each f℥iss (6.00 c.c.).
Ol. ricini ..... f℥ij (8.00 c.c.).
Aquæ cologniensis . f℥j (30.00 c.c.).

Sig.: Brush in vigorously each day.

Instead of lotions, ointments such as the following may be employed:—

℞ *Betanaphthol* ..... ℥j (4.00 Gm.).
Vaselini ..... ℥j (31.00 Gm.).
Ol. bergamott. ..... ♏xl (2.46 c.c.).
Sig.: Rub in twice a day.

An efficient treatment consists in the swabbing of the bald areas once or twice a week with

℞ *Acidi carbolici,*
Spts. vini rect., of each f℥ss (15.00 c.c.).

Or, 50 per cent. **trikresol** may be employed.

Within recent years I have employed a **chrysarobin ointment** which has given me more uniformly good results than any other topical application:—

℞ *Chrysarobini* ..... gr. x-xxv (0.65-1.62 Gm.).
Lanolini ... ℥j (4.00 Gm.).
Adeps benzoat. .... ℥vij (27.21 Gm.).
M. Rub in in small quantity. Protect the eyes from contact with ointment.

The routine treatment adopted by the writer is of an antiseptic nature. The head is washed daily for several minutes with a strong **tar soap,** which is then sluiced off and the head dried. Then the scalp is treated successively with 2 per cent. **sublimate solution, absolute alcohol,** with the addition of ½ to 1 per cent. **naphthol,** and finally with 2 per cent. **salicylic acid in oil.** In all moderately fresh cases the disease is brought to a standstill at once. O. Lassar (Dermat. Zeit., Sept., 1900).

Cases under the author's observation that were benefited or cured by applications of **chrysarobin ointment,** 10 to 15 per cent. strength, used daily for a week or ten days, followed by pure **carbolic acid** applied lightly with a swab. The ointment referred to sets up considerable inflammation, and must be used cautiously. When this inflammation has subsided, areas here and there the size of a silver dollar are touched from time to time with the acid. The results in the cases given were highly satisfactory. E. J. Emerick (Columbus Med. Jour., Feb., 1901).

A preparation of 30 per cent. of **chrysarobin** applied for two to eight weeks in alopecia areata causes vascular dilatation, thickening of the vascular walls, proliferation of the perithelial cells, infiltration of the connective tissue round the vessels, and hypertrophy of the connective-tissue cells. Numerous mast cells were seen round the vessels. In some places there were polynuclear leucocytes, but no agglomeration of lymphocytes. In the upper layers of the epidermis there was edema, with the formation of parakeratotic desquamative lamellæ, and in the deeper layers there was proliferation of the prickle cells round the follicular orifices, which gives rise to the formation of the cellular sheaths, in the center of which new hairs form. By repetition of the chrysarobin irritation this cellular proliferation is repeated till new follicular sheaths are produced. New sebaceous glands are also formed laterally. Finally, new arrector muscles form and new papillæ, in which develop new hairs. Hodara (Jour. des mal. cut. et syph., Sept., 1903).

The following treatment has given the most satisfactory results: Every night for one week the affected spots should have well rubbed into them an ointment of chrysarobin, of a strength of from 20 grains to 2 drams of the drug to 1 ounce of petrolatum. If the disease is not checked this treatment should be repeated. After the disease has stopped spreading, precipitated sulphur ointment (1 to 2 drams to the ounce) should be used. Severe or chronic cases may call for other measures. Dillingham (Amer. Med., Mar. 12, 1904).

Case of a young girl in which there was a circular patch three inches in diameter on the scalp at the side of the occiput, hairless, smooth, and shining. The treatment consisted in painting it with a 30 per cent. solution of **formaldehyde.** This was done every day for the first week or two, until signs of inflammatory reaction appeared. The treatment was then suspended, and a sedative ointment applied. When the inflammation subsided the formalde-

hyde was again continued, stopping the application as soon as inflammatory trouble appeared. This routine of treatment was persevered in for about six or nine months. About this time a growth of hair made its appearance, continued to grow, and in every way corresponded with the surrounding hair. One year after cessation of treatment the growth of hair was continuing in a perfectly normal way. J. J. McInerny (Brit. Med. Jour., Jan. 25, 1908).

The **faradic current** applied with a wire brush electrode is often useful, as is likewise the use of **high-frequency currents.** In obstinate cases blistering of the affected areas may be resorted to.

PHOTOTHERAPY.—Many writers, including Finsen, Hyde, Montgomery, Kromayer, and others, have testified to the value of **actinic light rays** in this disease. It is admitted that many cases in which light is used might have recovered spontaneously. Kromayer's results, however, in cases of extensive and even total alopecia of years' standing indicate that light therapy is one of the most useful measures in the treatment of this disease.

The iron arc or carbon arc may be employed. The ordinary London Hospital type of lamp suffices for this purpose and permits of the exposure of an area the size of a silver dollar. Reaction varying in degree from an erythema to the formation of a blister results at the end of some hours. The same area can be again treated after a lapse of two or three weeks.

Cases illustrating the rapid improvement under phototherapy with the **ultraviolet rays.** Success was obtained in many cases in which previous measures applied for months had failed to benefit. Joachim (Deut. med. Woch., May 13, 1909).

Piffard's iron spark-gap lamp—a small lamp made of rubber with a handle to hold it—recommended. For use it is attached to a coil. The quartz lens is removed in treatment, as it allows only ultraviolet rays to pass through. The lamp is held just far enough away from the scalp to prevent sparking, and continued for five to ten minutes, and the application is repeated in two to four days. Heat is thrown out by the lamp and the skin gets reddened. G. T. Jackson (Jour. of Cutan. Dis., Jan., 1910).

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ALSOL. See ALUMINUM: ALUMINUM ACETOTARTRATE.

ALUM (*Alumen*).—The alum used in medicine is, chemically, the double sulphate of aluminum and potassium [$AlK(SO_4)_2 + 12H_2O$]. It occurs in large, octahedral, translucent crystals, or as a colorless powder, odorless, but with a sweetish, strongly astringent taste. When left in an open bottle, the salt becomes whitish on the surface, owing to the absorption of ammonia from the air. Dried, "burnt," or exsiccated alum (*Alumen Exsiccatum*), *i.e.*, alum from which the water of crystallization has been driven out by heating, occurs as a white, granular, strongly hygroscopic powder.

DOSE.—The dose of alum for internal use (rarely employed) is 5 to 30 grains (0.03 to 2.0 Gm.); the average dose is 7½ grains (0.5 Gm.). To secure an emetic effect, 1 to 2 drams (4 to 8 Gm.) must be given.

MODES OF ADMINISTRATION.—Alum is soluble in 9 parts of cold water (the saturated solution thus containing, roughly, 10 per cent.), and in 0.3 parts of boiling water. It is completely insoluble in alcohol, but dissolves readily in warm glycerin. Dried

alum, possessing greater concentration than the crystalline form, requires more water for dissolution—17 parts of cold and 1.4 parts of boiling water. When exhibited for other purposes than as an emetic, alum is best given in a flavored syrup, *e.g.*, syrup of orange peel. When it is used to secure emesis, a small amount of simple syrup may be employed as vehicle. The subsequent ingestion of warm water augments its emetic effect. For astringent gargles, sprays, anhydrotic lotions, and rectal or vaginal injections, solutions containing 2½ to 20 grains (0.15 to 1.2 Gm.) of alum to the ounce (30 c.c.) of water should be prescribed. When an astringent eye-wash is desired, 2 or 3 grains (0.12 to 0.20 Gm.) of alum to the ounce of water may be used. The "alum curd," made by adding to a pint (473 c.c.) of milk 2 drams (8 Gm.) of alum, boiling the mixture, and straining off the curd, is also a useful preparation for this purpose. Dried alum, being anhydrous, is especially adapted for use as a dusting powder, for insufflation, and in ointments. It is applied to superficial growths as an escharotic. A glycerite of alum is official in the British Pharmacopœia.

INCOMPATIBLES.—The salts of aluminum, including alum, are incompatible with the alkalies and carbonates of the alkali metals; with the tartrates; with tannic acid, and with salts of iron, mercury, and lead.

CONTRAINDICATIONS.—In individuals subject to bronchial irritation, the long-continued use of alum is inadvisable, in view of the exciting effect it exerts on these structures.

PHYSIOLOGICAL ACTION.—When applied externally alum causes hardening of the skin, or, if used in concentrated solution, exerts a slight caustic effect. Whenever it is brought in contact with albumin, as occurs when it is applied to a denuded area, the albumin is coagulated. The precipitate is soluble, however, if an excess of albumin be present. The *astringent* and *antiseptic* effects of alum and other aluminum salts depend upon this coagulating property. Their power of penetrating into tissue-cells is, however, very limited (Siem).

Small doses of alum taken orally at first stimulate the flow of saliva, then reduce it through their astringent effect. The buccal mucosa becomes whitish and shriveled, owing to coagulation of the albuminous constituents, and the enamel of the teeth is likely to crack in places. On reaching the stomach, the drug causes a decrease in the amount of gastric juice secreted, and coagulates the pepsin. A similar effect being exerted in the intestinal canal, constipation results. In larger doses, the *emetic* effect of alum becomes manifest, and a *purgative* effect may also be noted.

UNTOWARD EFFECTS AND POISONING.—The injurious effect of alum on the teeth may be avoided (1) if care be taken to cleanse them well at once after employing an alum gargle or mouth-wash; (2) by limiting the use of alum to applications of a strong solution or of the solid salt in all cases in which local astringent effects will suffice. The unfavorable action of alum when long employed by persons subject to bronchial irritation has already been referred to.

Large amounts of alum taken internally cause nausea, vomiting, pain in the abdomen, and diarrhea, owing to the inflammation of the gastrointestinal mucosæ produced through the cellular albumins.

Case in which, through gargling with a concentrated alum solution, a portion of the fluid was accidentally swallowed. This was followed by severe abdominal pains, vomiting of mucus and blood (39 times), and voiding of blood-stained urine. Recovery only after the lapse of thirteen days. Kramolin (Therap. Monatsh., 325, 1902).

Alum baking powders and pastry to which alum has been added in order to whiten the product are possible sources of gastrointestinal irritation, though the amount of aluminum liberated, at least in the case of bread baked with alum powders, is often so slight as to be of doubtful importance.

THERAPEUTIC USES.—As an Astringent.—This is the chief use of alum. Combined with it is an antiseptic effect, which is also of value.

In all catarrhal and relaxed states of the mucous membranes, as well as in certain skin affections, alum is beneficial when locally applied. Aqueous solutions of from 5 to 20 grains to the ounce (1 to 4 per cent.) strength are chiefly employed; stronger solutions induce undesirable secondary irritation.

In **catarrhal throat affections** fluid preparations containing alum (1 to 5 per cent.) form a useful gargle or spray. Since alum is injurious to the teeth, the mouth should be washed out, preferably with some alkaline solution, after using this drug. A glycerite of alum (10 to 20 per cent. solution of alum in glycerin, the preparation of which is greatly facilitated by heating) is very efficacious when applied locally in **subacute pharyngitis** and **laryngitis**, especially where a tendency to edema of the tissues involved is present. For the relief of **hoarseness** or of **tickling sensations** in the throat, a mixture of equal parts of powdered alum and sugar, placed on the tongue and allowed slowly to dissolve, is productive of benefit (Bunnell).

In **acute coryza** alum has been incorporated in snuff, to which it imparts astringency. The following preparation is suitable for use in the early stages of coryza:—

℞ *Alum* ..... 3 grs. (0.2 Gm.).
Morphine sulphate . 2 grs. (0.13 Gm.).
Cocaine hydrochloride ..... 1 gr. (0.065 Gm.).
Camphor,
Bismuth ....of each 2 drs. (7.77 Gm.).

M. bene. Sig.: To be used as snuff every two hours; a small quantity in each nostril.

In **follicular tonsillitis** and **diphtheria** alum in pencil form may be applied to the involved surfaces with benefit.

In **conjunctivitis** alum may also be used. A 0.5 per cent. solution may be used as a lotion, or the alum curd, made by the addition of powdered alum to milk or white of egg until a curdy mass is formed, may be applied to the eye every two hours. Similar applications prove effective in **ecchymosis of the eyelid** (black eye). In **gonorrheal ophthalmia** alum has also been used in a solution containing 6 grains of the salt in 1 ounce of water, applied four times daily. In **granular conjunctivitis** a crystal of alum may be drawn over the involved mucous surface after turning the lid (Bunnell).

In salivation or **ptyalism** of mercurial origin a 4 per cent. solution of alum may be employed for its astringent action.

In the treatment of **night-sweats**, or in sweating of the hands and feet (**hyperidrosis**), washing the skin surfaces with a 0.5 per cent. solution of alum will markedly improve the condition.

In **chilblains** a 4 per cent. solution of alum has been applied with benefit.

In **gonorrhea** and **leucorrhea** alum has been used as an astringent injection or douche in ½ to 2 per cent. strength.

In **pruritus vulvæ** a 4 per cent. solution of the salt will not infrequently relieve the itching.

In **ingrowing toenail** with granulations absorbent cotton soaked in a 6 per cent. solution of alum may be introduced under the edge of the nail.

In **chronic dysentery** a 1 per cent. solution of alum is sometimes employed as a rectal injection.

As a styptic alum is likewise an effective agent.

In **epistaxis** it will often act promptly. Pledgets of cotton should be dipped in a saturated solution of alum and packed in the bleeding cavity; they may be left in until all danger of recurrence has passed—generally about twelve hours. In minor degrees of hemorrhage the alum solution may be sprayed in, or powdered alum may be used as snuff or introduced by means of an insufflator.

Similarly, in hemorrhage succeeding upon the **extraction of teeth**, the placing in the cavity of cotton dipped in a saturated solution, or the introduction of powdered alum, will often be effective in arresting the bleeding.

In **hemoptysis** a fine spray of 5 per cent. alum solution is claimed to have been productive of benefit.

In the **intestinal hemorrhage of typhoid fever** alum has been recommended by many clinicians, Whitla in particular. It is believed to do good in this condition through its antiseptic properties, as well as through its astringency.

In **uterine hemorrhage** of all kinds alum is a useful styptic. It may be employed as an injection in the strength of 1 dram to the pint, or, as R. Beverly Cole recommended, an egg-shaped piece of alum may be inserted into the uterine cavity. Not only is the styptic effect produced, but the tissues of the uterus are stimulated and the organ is caused firmly to contract.

As a Caustic.—Dried ("burnt") alum, which exerts an escharotic effect, owing to the fact that in addition to the inherent properties of alum it withdraws water from the tissues, may be applied to **exuberant granulations, condylomata, chronic conjunctival inflammations**, etc.

Burnt alum may also be used as a dressing for **sluggish ulcerations** and as an application to **swollen gums** and in **ulcerative stomatitis** (Bunnell).

As an Emetic.—In doses of 1 or 2 drams alum has been used as an emetic, especially in the treatment of **croup** in children. A teaspoonful of the salt may be dissolved in 6 tablespoonfuls of a mixture of syrup and water, equal parts, and administered every fifteen minutes.

This sometimes serves quickly to arrest an impending attack of croup, the astringent effect of the salt upon the mucosa of the throat contributing in the benefit by counteracting the local hyperemia.

As a Stimulant to Peristalsis.—In doses of ½ dram every four hours alum has been found to induce purgation. The large amount of watery fluid thrown out from the mucosæ in the presence of alum apparently obviates its irritating influence on these membranes. In **tympanites** due to **peri-**

toneal inflammation succeeding upon abdominal operations in cases suffering from infective states of the abdominal viscera, the high rectal injection of an ounce of alum in a quart of water has been found effectively to excite contractions of the paretic gut.

Case in which Epsom salt, calomel, soap and water, castor oil, glycerin, turpentine, and oxgall were successively used without avail. A solution of an ounce of powdered alum in a quart of warm water was injected into the rectum, and in ten minutes flatus escaped from the rectum. In an hour the enema was repeated successfully. The patient was practically convalescent on the following day. Since this case, the author has used the alum enema in hundreds of cases, and always with good results. Sometimes it is necessary to repeat the injection before it will act, and this can be done with safety an indefinite number of times.

There is sometimes some pain, not severe, attending its use. Injected like any other enema, probably in no instance does it go above the sigmoid flexure. The throwing off by the bowel of a tubular cast is of no importance, as it is composed simply of mucus whose albuminous elements have been coagulated by the alum.

The alum seems to have as specific an action in inducing intestinal peristalsis as has castor oil when taken into the stomach. It does not produce a serous exudation from the intestinal walls, and for that reason the author prefers it to Epsom salt when the stomach will retain it. During nine years in which alum enema was used, percentage of mortality in abdominal work has been a little less than one-half of what it was during the preceding seven years. Hardon (Amer. Jour. of Obstet., June, 1901).

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ALUMINUM (*Aluminium*). — A bluish-white, silvery metal, noted for its low specific gravity (2.7) and its unalterability on exposure to the air.

The most important of the compounds of the metal aluminum employed in medicine, viz., the double sulphate of aluminum and potassium, has already received separate consideration (*v.* Alum). Numerous other salts have been used, chiefly externally, as astringents and antiseptics.

Taken internally, the salts of aluminum are, according to some observers, not all absorbed from the gastrointestinal tract, this accounting for the fact that no functional disturbances in the organism at large occur as a result of their ingestion. According to others, however, alum (and probably other salts) is absorbed, in extremely small amount, in the alimentary canal, and is eliminated with the bile and urine. When administered experimentally to animals by subcutaneous injection, soluble salts of aluminum cause no symptoms at all until several days or even weeks later (Siem), when the metal is no longer present in the circulation. In mammals the symptoms appear in from three to five days, and are in many ways similar to those of subacute arsenic poisoning. The animal shows loss of appetite, obstinate constipation, emaciation, and languor. Next there appears vomiting. Voluntary movements, executed only upon coercion, are attended with trembling and twitching. Sometimes there is general tremor or convulsive twitching, and sometimes extreme weakness or partial paralysis of the posterior limbs. There is complete loss of sensibility to pain, though consciousness is retained. Finally, control of the tongue and the power

of swallowing are completely lost, saliva dribbling from the mouth. The symptoms correspond precisely to those of human acute bulbar paralysis. Such phenomena never result from the oral use of aluminum salts, even where long continued (Sollmann). Diarrhea and albuminuria appear before death. On post-mortem examination the gastrointestinal mucosæ are found hyperemic and swollen, and the kidneys and liver frequently show fatty degeneration, the former presenting, in addition, cortical hemorrhages.

Following are some of the more important salts of aluminum employed in medicine:—

Aluminum Hydroxide (*Alumini Hydroxidum*), $Al(OH)_3$, made by precipitating a soluble salt of aluminum with an alkali or alkaline carbonate. It occurs as a light, amorphous, colorless, tasteless powder, soluble in acids and alkalies. It is used as an astringent in **inflammatory skin affections.**

Aluminum Sulphate (*Alumini Sulphas*), $Al_2(SO_4)_3+18H_2O$, prepared from the hydroxide by dissolving it in dilute sulphuric acid. It occurs as a white, crystalline powder or in larger crytals or pencils, and, like alum, has a sweetish and astringent taste. It is freely soluble in water, and has been used for much the same purposes as alum itself, viz., as an astringent, antiseptic, and caustic in the treatment of affections of the nose and throat, including **enlarged tonsils** and **nasal polypi**; of the uterus, including **endometritis**; as a lotion for **foul ulcers**, and in vaginal conditions associated with offensive discharges. The strength of the solutions used is the same as with alum.

The following aluminum compounds are non-official:—

Aluminum Acetate (basic), $Al_2O_3 4C_2H_3O_2 + 4H_2O$. Obtained in solid form from its solutions by rapid drying on glass at a low temperature, this salt occurs as a colorless, crystalline or amorphous powder which is insoluble in water. It is antiseptic and astringent, and has been used internally in **dysentery** in doses of 5 to 10 grains (0.3 to 0.6 Gm.). An 8 per cent. solution of aluminum acetate is known as "liquor Burowii," which has been extensively used as an application in **skin affections**, and in **suppurating wounds.** One to 3 per cent. solutions are useful as a mouth-wash, and are particularly effective in overcoming **fetid breath.** In a solution of 1 to 150 strength, this salt of aluminum may be used as an astringent enema in affections calling for such a measure.

> Antiseptic properties of moist applications of a solution of aluminum acetate used quite generally by the author after operations where there is the slightest danger of infection. The solution is also invaluable in the mouth, particularly for necrosis and suppuration, where it does more good than mouth-washes. An excellent method of treating **tears of the perineum**, after confinement, is to apply gauze saturated with the solution, and to have the patient lie on the abdomen for a few days. F. Weitlaner (Klin. therap. Woch., Nu. 6, 1908).

> Usefulness of aluminum acetate solution emphasized. For certain surgical purposes this is one of the best antiseptic solutions, though it is unknown to most surgeons and practitioners. **Burns** may be treated with dressings wetted with a 1 per cent. solution of aluminum acetate. This solution, while antiseptic, is also non-toxic, non-irritant, and yet markedly astringent. It is not to be employed in surgical operations, as it spoils steel instruments; but

as an antiseptic for moist fomentation of **wounds** that are **infected or probably unclean**, or as a medicament for a bath in which to place an infected hand or foot for continuous irrigation, it is to be strongly recommended. The common strength is that of 1 dram of the liquor aluminii acetatis of the German Pharmacopœia (a 7½ per cent. solution) to 1 fluidounce of water. There is no danger of poisoning from it. By the employment of continuous irrigation by means of a bath of the 1 per cent. solution, pyogenically infected hands and feet, which but for the action of the solution would have called for amputation, have been saved. For **dermatitis**, whatever its cause; for **suppurating open wounds**, and for cutaneous **erysipelas**, much is to be said for the favorable results obtained. One objection that should be mentioned is that after three weeks of continuous irrigation of a member such as the hand the surface tissues may assume a ligneous hardness. M. F. Waterhouse (Hospital, Aug. 27, 1910).

Aluminum Acetotartrate (Alsol), prepared by mixing a 5 per cent. solution of basic aluminum acetate with a 2 per cent. solution of tartaric acid and evaporating to dryness. It occurs in colorless crystals, or in whitish amorphous masses having a slightly acid, astringent taste. It dissolves slowly, but completely, in water, but is insoluble in alcohol and ether.

This substance has an action similar to that of aluminum acetate, and is one of the best of the aluminum salts used in medicine. It has been employed largely, though not exclusively, in **diseases of the respiratory passages**. Thus in 0.05 to 2 per cent. solutions it has been used as a nasal douche. Mixed with 2 parts of powdered boric acid it may be used as a snuff. In **tonsillitis** a 1 per cent. solution of it makes a suitable gargle. Strong solutions (*e.g.*, 50 per cent.) have been employed with advantage in the treatment of **chilblains** and **skin diseases** of various kinds—also in **wounds** as disinfectants. Eye affections, such as **ophthalmia neonatorum**, **chronic** types of **conjunctivitis**, etc., have also been treated with this salt.

In a 5 per cent. solution, alsol inhibits the growth of gonococci, streptococci, and anthrax bacilli. In the treatment of **wounds**, it is astringent, disinfectant, and antiseptic and does not irritate the tissues. In a 1 per cent. solution, it is useful as a gargle in **tonsillitis**. J. W. Frieser (Wiener klin. Rundschau, Aug. 12, 1900).

Alsol in a 5 per cent. solution destroyed the spores of **anthrax** in ten hours, acetate of aluminum in an 8 per cent. solution in two hours, while carbolic acid in a 5 per cent. solution had no effect whatever on their development. In the case of *Streptococcus pyogenes, Staphylococcus pyogenes aureus,* the gonococcus, and the tubercle bacillus, however, carbolic acid has a greater bactericidal power than acetate of aluminum. The combination of the acetate with the tartrate greatly raises the bactericidal power, so that alsol is considerably more potent than carbolic acid. Aufrecht (Deut. aertzl. Zeitung, Feb., 1900).

Alsol exerts an action similar to the acetate of aluminum. It is said to possess a somewhat stronger disinfectant action than the same strength solution of carbolic acid, and is mildly astringent at the same time. The author employed it in a concentration of from ¼ to ½ per cent. Finding that warm and cold compresses are of value in the treatment of certain eye affections, he attempted to extend their use by employing alsol. In **blennorrhœa neonatorum** he washed the eyes out every half an hour, both during the day and night, and obtained excellent results. The direct forms of treatment, *e.g.*, painting with silver nitrate, etc., must be carried out as well, the alsol solution only acting as a disin-

fectant and mild astringent. In **acute conjunctivitis** and **acute granuloma** cold compresses applied for ten to twenty minutes three or four times a day found of value. The same results were obtained in **chronic conjunctivitis** and **chronic trachoma.** In **scrofulous ophthalmia** warm compresses were applied three times a day for about half an hour. In **hordeola** and in **ulcers of the cornea, iritis,** etc., satisfactory results were obtained with alsol. L. Pick (Therap. Monats., July, 1903).

Aluminum Boroformate, prepared by saturating with freshly precipitated and well-washed aluminum a solution of 2 parts of formic acid and 1 part of boric acid in 6 or 7 parts of water. It occurs in pearly scales, which are hygroscopic and dissolve completely, though slowly, in water. Its solution has a sweet, faintly astringent taste, and does not coagulate solutions of albumin. Martenson in 1894 recommended this salt strongly for use as a gargle in the **throat affections in children,** preferring it to all other preparations of aluminum.

Aluminum Borotannate (Cutal), a product of the reaction of tannic acid with borax and aluminum sulphate. It is a brownish insoluble powder, which combines with tartaric acid to form **Aluminum Borotannotartrate** (soluble Cutal).

This salt, in common with the other aluminum compounds, is antiseptic and astringent. It has been used chiefly in skin affections and is recommended particularly in **weeping eczema** and **pruriginous** affections. The following formula may be employed:—

℞ *Aluminum borotannate* ..... 1 dr. (4 Gm.).
Olive oil ..... 2½ drs. (10 Gm.).
Lanolin..to make 10 drs. (40 Gm.).

When the flow of secretions has been arrested, the drug may be used with advantage as a dusting powder in the following mixture:—

℞ *Aluminum borotannate,*
Zinc oxide,
Powdered talc, of each ..... 2½ drs. (10 Gm.).

In **hemorrhoids** Koppel has recommended the use of an ointment containing 10 per cent. of cutal, and in **fissures** of the hands of one formulated thus:—

℞ *Cutal* ..... ¾ dr. (3 Gm.).
Oil of sweet almonds,
Lanolin ..of each 3¾ drs. (15 Gm.).
Orange-flower water ..... 2½ fl. drs. (10 Gm.).

Aluminum borotannotartrate, or soluble cutal, has been used in the treatment of **second-degree burns,** as a 10 per cent. solution in glycerin in **follicular throat affections, in catarrhal metritis, in hemorrhoids,** and in **gonorrhea.**

Aluminum Borotartrate (Boral), a combination of aluminum, boric acid, and tartaric acid. It occurs as white crystals having a sweetish, astringent taste, and is freely soluble in water. It is useful in **inflammatory diseases** of the **nose** and **nasopharynx, in erysipelas,** and, in solution with tartaric acid, has given good results in **gonorrhea.** It may be employed either alone in watery solution or in glycerinated mixtures.

Aluminum Carbonate, $Al_2(CO_3)_2$, occurring in chalky-white, easily powdered, tasteless masses. According to Gawalewski, it constitutes an extremely mild styptic and astringent, and is hence better adapted than are burnt alum and other aluminum preparations in the treatment of **ocular**

affections, croup, diarrhea, hemoptysis, skin eruptions, and hyperidrosis.

Aluminum Chloride, $Al_2Cl_6 + 12H_2O$, a yellowish granular, crystalline, hygroscopic powder, soluble in water, alcohol, and ether. It has been used internally in tabes in doses of 1½ to 4 grains (0.1 to 0.25 Gm.), and externally as a disinfectant.

Aluminum Phenolsulphonate (Sulphocarbolate), $Al_2(C_6H_4HSO_4)_6$, a reddish powder with weak phenol-like odor and a strongly astringent taste, soluble in water, alcohol, and glycerin. It has been recommended as a substitute for iodoform in the treatment of superficial, circumscribed, suppurating lesions, and of cystitis.

Aluminum Salicylate, $Al(C_6H_4OHCOO)_3$, a reddish powder, insoluble in water and alcohol, soluble in alkalies. Used as an antiseptic powder for insufflation in catarrhal states of the nasal and pharyngeal mucous membranes, and in ozena.

Aluminum Silicate, $Al_2Si_3O_9$, a white substance, insoluble in water and acids. It has been recently recommended in the treatment of gastric hyperacidity and hyperesthesia.

> Investigations of the action of silicate of aluminum upon the gastric secretions and upon disease symptoms resulting from abnormalities of secretion. Under the name *neutralon*, this substance occurs as a fine, tasteless, odorless, and insoluble powder. Taken into the stomach it reacts with the excess of hydrochloric acid to form silicic acid and aluminum chloride. The latter acts as a protective and astringent to the gastric mucosa in a manner similar to silver nitrate and bismuth, and has no toxic effect. In all cases of hyperacidity or hypersecretion, whether of neurotic origin or due to organic disease or injury, the remedy was found to be very effective in reducing the acidity, relieving pain, and aiding digestion. Results especially good in persistent cases of hypersecretion with motor insufficiency. Gastric hyperesthesia associated with anemia and chlorosis favorably influenced in several instances. Excessive acidity in cases of gastric ulcer was also reduced. The drug was given in doses of ½ to 1 teaspoonful in 3 ounces of water, one-half to one hour before meals. No untoward symptoms. Rosenheim and Ehrmann (Deut. med. Woch., Jan. 20, 1910).
>
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ALUMNOL, the aluminum salt of betanaphthol-disulphonic acid $[Al_2(C_{10}H_5OH(SO_3)_2)_3]$, is made by adding a solution of barium naphthol-disulphonate to one of aluminum sulphate, filtering off the precipitate of barium sulphate, and evaporating to dryness. It contains about 5 per cent. of aluminum, and occurs as a fine white or slightly reddish, non-hygroscopic powder with a sweetish, astringent taste. It is readily soluble in cold water and in glycerin, slightly so in alcohol, and is insoluble in ether. On exposure to the air it becomes darker in color, by virtue of its reducing properties.

MODE OF EMPLOYMENT.—Alumnol is employed chiefly in solution, though also frequently as a dusting powder. As a mild astringent and antiseptic it is used in solutions of 0.5 to 5 per cent. strength. For caustic effects, a 10 or 20 per cent. solution may be employed. Where the action of several antiseptics at once is desired, alumnol may be used in combination with agents such as corrosive sublimate, resorcin, etc.; it is incompatible, however, with silver nitrate or other reducible salts, as well as with alkalies.

THERAPEUTIC USES.—The almost unirritating and non-toxic qualities of alumnol in weak solutions render it available as an astringent and antiseptic for the treatment of chronic catarrhal processes, and also in sluggish ulcerations. In acute cases, however, it generally proves too irritating to be of value. It has been employed mainly in gynecology and gen-

itourinary surgery, and, to a less extent, in general surgery, laryngology, and dermatology.

In ½ to 1 per cent. solution alumnol was found useful by Heinze and Liebreich in **gonorrheal endometritis** and in **colpitis** not of gonorrheal origin. Kontz, employing alumnol in a series of 16 gynecological cases, found that **cervical catarrh** and **simple perimetritis** yielded to its repeated use, and that **gonorrheal vaginitis** was readily cured by it. In endometritis accompanied by adnexal lesions, however, pain was augmented, owing to the irritation.

This author employed a 3 per cent. solution for lavage, a 10 per cent. solution in the treatment of **endometritis** and **erosions,** and powders and bougies of 20 per cent. strength. Marfan used 3 per cent. bougies of alumnol in **vulvovaginitis.**

Intra-uterine injections of the iodide of alumnol have been recommended by Grammatikati as a **substitute for curettement** of this organ.

Though alumnol has been claimed to exert a peculiarly destructive action on gonococci, its use as an injection in **gonorrhea** in the male has not led to results commensurate with early expectations. Casper employed it in 12 cases of acute gonorrhea, 20 chronic cases, 4 cases of gonorrheal epididymitis, 2 of post-gonorrheal adenitis, and 2 of soft chancre, administering intraurethral injections of 0.25 to 2.0 per cent. solutions; he did not find it superior to other drugs in general use. Samter confirmed these findings, though Chotzen claimed to have obtained good results. In the cases of **soft chancre** in Casper's series healing was promoted by the application of alumnol. Asch used a 10 to 20 per cent. solution for cauterizing the lacunæ and crypts at the urethral orifice.

As a surgical antiseptic, alumnol is used in 0.5 to 3 per cent. solutions. In the dressing of **wounds** and in **ulcerations,** specific or non-specific, Eraud found it to produce no irritation or pain. As a desiccant powder for wounds this author considers it efficacious.

In nose and throat practice, alumnol has been found valuable in **simple chronic** and **hypertrophic rhinitis,** in **ozena,** in **catarrhal** and **follicular tonsillitis,** and in acute and **chronic pharyngitis.** It is used either in a 1 per cent. solution as a douche, in a watery glycerin solution (1:5), to be applied to the affected parts, or as a powder, mixed with starch (10 to 20 per cent.), for insufflation. Stepanicz found that in acute laryngeal affections the **roughness of voice** generally disappeared after a single inhalation of a 1 per cent. solution. In chronic cases, insufflations of alumnol and starch (2 to 10 per cent.) also gave good results. Metzerott used alumnol with satisfaction not only in laryngitis, pharyngitis, tonsillitis, and peritonsillitis, but also in **edema, syphilis,** and **tuberculosis of the larynx.** In a case of symptomatic laryngeal edema, probably of syphilitic causation, with a severe grade of stenosis, the administration of alumnol solutions in the form of injections and the steam spray made it possible to defer tracheotomy for six months. In the case of a singer troubled with **subglottic laryngitis,** with wave-like fluttering of the vocal cords, an alumnol spray gave early relief; also in one of **chorditis nodosa** (singer's nodules), strong solutions of the remedy proved beneficial.

In otology alumnol has also been employed. In **suppurative otitis media** Heath noticed, however, that it sometimes caused persistent burning sensations, and that it tended to unite with pus in the external meatus to form stone-like pellets,—a peculiarity condemning its use in this disorder.

In dermatology alumnol has been found serviceable in powder form (12 to 25 per cent.), collodion (5 to 10 per cent.), and ointment (1, 5, and 12½ per cent.). It has proven effective in **dermatitis, acute eczema** of all sorts, and **chronic eczema,** but in syphilis and the parasitic skin affections did not yield much benefit. In **acne** and **acne rosacea** as good results have been obtained with it as by most other methods of treatment. Chotzen found alumnol efficacious in acute and chronic inflammations of the skin and mucous membranes, including **erysipelas, favus, lupus, soft chancre,** and **erosions.** Eraud made the statement that alumnol appeared to be useful in certain varieties of **pruritus,** especially of the anus and scrotum. S.

AMAUROSIS.—DEFINITION.—Amaurosis, formerly used to designate partial or complete blindness, has become, since the common employment of the ophthalmoscope, much more limited in its meaning and application. At present, imperfect vision not due to errors of refraction or visible pathological changes may be classified under "amblyopia"; complete blindness of one or both eyes and usually that form of blindness caused by disease of the nervous apparatus of sight, the retina, optic nerve, and cerebral centers under amaurosis.

[Both words should be so used that they refer only to certain kinds of blindness which are to be described by a preceding adjective, and unless thus defined their meaning is vague and uncertain, carrying no suggestion of etiology or pathology. When the media of the eye are transparent, normal or abnormal conditions of the fundus are as easily diagnosed by the expert ophthalmologist as are diseases of the skin by the dermatologist; therefore, except as a convenience or as a substitute for the word blindness, amaurosis might well be omitted from ocular vocabulary. Eyes blinded by disease of or traumatism to the middle or anterior third are seldom described as amaurotic eyes. H. F. HANSELL.]

Amaurosis in Brain Disease.—Tumors or other organic changes in the brain by which the optic tract is directly compressed or the ventricular fluid is forced into the optic nerve sheaths will produce blindness. The process is a mechanical one. In the former the optic nerve fibers in the tracts are directly compressed and deprived of their function; in the latter, the optic nerve is surrounded by fluid contained within a sac of only moderate distensibility. The gradually induced compression of the nerve induces arterial anemia and venous congestion of the nerve-head and retina, which is soon followed by serous and solid exudation into the distal extremity of the nerve. Finally the optic nerve fibers become atrophied from stoppage of circulation and pressure of exudation. The loss of vision may commence in the periphery of the field and advance by slow stages toward the center until finally the entire field is wiped out; or, as may be the case in apoplexy, a section of the field, one-half, one-quarter, or less, or the region about the fixation point and including it, is suddenly lost. Continuation or extension of the brain lesion will be followed by loss of the entire visual field.

Amaurosis in Nephritis.—Disturbance of vision may be caused by hemorrhage or edema into the cerebral centers, by pressure upon the chiasm or tracts, or by the action of the poison of uremia, by which the brain functions are held in abeyance. In the first and second it may affect one or both eyes and be partial or complete. In the third it comes on rapidly, involves both eyes, and disappears in a few hours or in a day or two. There are no ophthalmoscopic changes visible in the retinal circulation or structural alterations in the nerve or retina. The blindness is strictly cerebral. In the early stages of hemorrhage or edema the eye-grounds are normal; later they show the signs of intracranial pressure. In a man who died twelve hours after cerebral hemorrhage and who was unconscious from the time of the attack until his death, the ophthalmoscope showed only moderate dilatation and tortuosity of the veins. These forms of amaurosis are not to be

confounded with the amblyopia of albuminuric retinitis, in which the vision is affected in several ways; by edema of the nerve-head, edema of the retina, hemorrhage in the foveal region, and patches of degeneration of that area. The diagnosis may be at once established by the ophthalmoscope.

Amaurosis in Hysteria.—Neuroses, the result of an unknown derangement of the nervous system originating within the body or of traumatism, may reduce or altogether destroy temporarily the visual power in one or both eyes, rarely the latter. The traumatism may be ocular or involve any other part of the body. In order to induce blindness or even amblyopia the causative disease or injury must affect an individual of peculiar or susceptible organization and makes manifest a tendency toward magnification of trifles for the sake of bringing into prominence the ego or for the sake of imposition. In traumatic cases the diagnosis between hysterical amaurosis and malingering is not always easy. Both offer no evidence externally or internally in the eye of any mark of injury or disease sufficient to account for the symptoms. In hysteria the well-known stigmata may be found—tubular field, transient and recurring ocular paralyses, reversal of the color field, well-defined patches of localized anesthesia of the skin, inexplicable and transient pains distributed anywhere and everywhere in the body and created by cleverly directed interrogation. The majority of the subjects are women who are more or less mentally unbalanced by disease of the sexual organs or by physical or mental idleness. The malingerer is usually a man who resorts to the excuse of blindness in order to avoid unpleasant or dangerous duty or to collect damages from a rich corporation. The symptoms of hysterical amaurosis are altogether subjective and of cerebral origin. The eyes cannot be held responsible.

> Commonly, in the recorded cases, there have been other manifestations of hysteria, but amaurosis may be the sole expression of this disorder. Unilateral hysterical amaurosis occurs rather more rarely than the bilateral form, according to Kron, and offers distinctive different diagnostic problems. But bilateral hysterical amaurosis is almost as rare an affection. The writer describes such a case which presents several interesting features: The sudden blindness, and later sudden menoplegia with loss of pain sense, the loss of stereognosis sense in the affected member due apparently to loss of muscular and articular sensation, and contracted visual fields of the tubular variety. The author reports 2 other cases. Diller (Jour. Amer. Med. Assoc., Apr. 24, 1909).

Amaurosis in Spinal Disease.—Primary atrophy of the optic nerves preceding or accompanying disease of the spinal cord and spinal nerves is a common affection. It is "primary" because it is initiated and carried to its finish without inflammation of the optic nerve visible to the ophthalmoscope. There is no edema or exudation. The disk margins remain clear cut and well defined. The first noticeable change is a loss of the normal pink color on the temporal half of the papilla and a diminution of the size of both the arteries and veins of the retina. Gradually the vascularity becomes less, the nerve becomes paler and finally white, all the fine vessels having become absorbed from the surface. Contemporaneously with the

atrophic process the vision declines until complete amaurosis results. Early in the disease the field for colors is concentrically contracted or the perception of green is lost, and the retina becomes less sensitive to light or the optic nerve less capable of transmitting feeble stimulation. The affection is binocular, although one eye is usually more affected. Secondary atrophy, that following inflammation of the intraocular end of the optic nerve, presents entirely different ophthalmoscopic appearances, and no confusion need arise in the diagnosis between the two affections. The diseases of which primary optic nerve atrophy is a prominent symptom are tabes, disseminated and lateral sclerosis, dementia paralytica, and paralysis agitans. The pupillary and visual disturbances may precede by many years the development of spinal affections, particularly posterior sclerosis, and many of the so-called idiopathic cases really belong to this class. The writer believes this is true also of paralysis agitans. He has at present a patient who seven years ago had incipient atrophy of the optic nerves with shallow excavation and for the past two years has slowly advancing paralysis agitans.

Amaurosis following Hemorrhage.—After extensive loss of blood from any cause, but especially from disease of the stomach, intestines, or uterus, blindness affecting both eyes, commencing two or three days after the hemorrhage and advancing rapidly, may ensue. The ophthalmoscope shows marked ischemia of the retina with low-grade edema of the nerve-head. The blindness may be complete and permanent, terminating in optic nerve atrophy; or, in an individual with good recuperative power or when the loss of blood has been moderate, restoration of sight may be complete.

Amaurosis in Pregnancy.—Toward the completion of the term of pregnancy or during confinement, vision may be entirely suspended in both eyes for some hours or days. The amaurosis is usually associated with convulsions or other signs of puerpural septicemia. It should be regarded as a strong indication of intense and general poisoning. The fundus either shows no deviation from the normal or the retinal veins are distended and dark in color, the nerve-head is slightly edematous, and an occasional hemorrhage is found in the retina. After safe delivery, vision rapidly returns and the eyes are restored to their previous condition. Atrophy of the nerve and permanent amaurosis as a result of pregnancy alone have not, as far as the writer knows, been described, yet he has seen cases in which no other cause for the blindness could be assigned.

> Case of amaurosis gradually developing in the course of pregnancy. The first signs of optic neuritis were noted about the fourth month; both eyes were affected and external causes could be excluded. The optic nerve was atrophied when the patient was first seen and the indications for interruption of the pregnancy were beyond question. Sight began to improve at once, and within two weeks vision was restored in the right eye. The other eye was first involved, and the nerve was atrophic beyond relief. The woman was a multipara of 37, with 8 children, and the author deemed it necessary to insure future sterility by an operation on the tubes. The case confirms anew the importance of immediate interruption of the pregnancy in case of optic neuritis from this cause. Holzbach (Zentralbl. f. Gynäk., May 23, 1908).

Case of a woman of 34, with chronic nephritis, who in the fifth month of her seventh pregnancy developed amaurosis with headache and detachment of the retina on both sides. Abortion was induced and was followed by retrogression of the detachment of the retina, but the atrophy of the optic nerve proved irreparable. The trephining to relieve the pressure on the brain evidently came too late; the pupil reaction was abolished by the second day after the woman had entered the hospital. The case teaches the importance of emptying the uterus and of prompt measures to reduce the intracranial pressure if vision is not promptly restored. Himmelheber (Münch. med. Woch., Oct. 19, 1909).

A form of amaurosis or amblyopia, not accompanied by ophthalmoscopic signs, or, at least, by none adequate to account for the condition, may supervene during pregnancy, parturition, or the puerperium. Rarely it may assume the form of a hemianopic defect or of a central scotoma in the fields of vision, and still more rarely of hemeralopia (night blindness). It is often associated with such signs and symptoms of toxemia as headache, edema, eclampsia, and scanty urine containing albumin, casts, and blood. It appears to form one of the rarer manifestations of toxemic poisoning. It is not proved to be dependent upon uremia, although it has usually been confused with so-called "uremic amaurosis." Recovery occurs, as a rule, completely within a few hours or days. Sydney Stephenson (Ophthalmoscope, March, 1910).

Amaurosis from Fracture of the Skull.—Numerous cases have been recorded of complete blindness of both eyes some months after a traumatism of the skull. The common lesion is fracture at the apices of the orbits with or without involvement of other bones at the base. Hemorrhage from rupture of a large blood-vessel either anteriorly at the base or involving the basal or cortical centers of vision, a frequent complication of fracture of the skull, will destroy vision.

In the latter lesion the amaurosis is more rapid in its onset and temporary. Absorption of the blood is followed by gradual return of vision unless the nerve structures have been destroyed by the insult or by pressure.

Transient blindness from contusion of the skull in a boy of 12 who had been run over by an automobile, brain substance protruding from a gash in skull. The boy was unconscious at first and was blind when he roused, the amaurosis being complete with no perception of light. Vision then gradually returned and by the third day was normal and it has persisted so to date, the other injuries soon healing. C. Hirsch (Deut. med. Woch., August 4, 1910).

Congenital and Hereditary Amaurosis.—Infants born with ocular or cerebral defects, such as buphthalmus, microphthalmus, or other deformities, or "amaurotic family idiocy," by which the essential parts of the eye or brain are wanting or so disturbed that function is absent, are hopelessly blind. Hereditary optic nerve atrophy, transmitted usually to males through the female line, appears suddenly between the twentieth and thirty-fifth year as a loss of central vision. The scotoma increases and the periphery of the field becomes contracted until the patient is permanently and totally amaurotic.

Having found in the family history of an inmate of the Missouri School for the Blind the presence of cataract in all the members of the family for at least five generations, the writer after receiving the opinions of 152 oculists concludes as follows: 1. All whose life work brings them into relationship with the blind should be aware of the dan-

gers connected with the marriage of a blind person. 2. The blind themselves should be warned of the danger to their children in case of marriage. 3. A distinction must be made between hereditary and non-hereditary forms of blindness. 4. Legal assistance should be invoked to prevent blind people from marrying. 5. This law should apply only to those cases of blindness in which heredity has been proved. With the exception of glaucoma and cataract, these diseases usually manifest themselves at or before the marrying age. 6. A law compelling every person to have an oculist's certificate before marriage, though idealistic, would be impracticable. 7. The general public should be educated in the dangers arising from hereditary blindness. C. Loeb (Annals of Ophthal., Jan., 1909).

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AMBLYOPIA. — DEFINITION. —The word "amblyopia" signifies, without specializing the cause, that the acuity of vision is below the normal. The degree of the loss of vision is not suggested by the word itself, nor has there been any attempt, as far as I am aware, to define its limitations. It has been inherited from the preophthalmoscopic times, when the two words amblyopia and amaurosis were commonly used, the former to mean dull vision and the latter, blindness.

[Today we seldom hear of amaurosis, but we have tenaciously held to amblyopia. Its use is convenient, but unless preceded by a descriptive adjective, such as toxic, hysterical, its meaning is indefinite and vague. The sense in which the word is properly used is to express partial loss of vision due neither to dioptric abnormalities nor to visible organic lesions, or, as expressed by the older writers, "amblyopia without ophthalmoscopic appearances." It is, therefore, not a disease, but a symptom, and is due to many causes. H. F. HANSELL.]

The varieties of amblyopia are usually classified into organic from toxic and intracranial causes, functional, exanopsia (disuse, non-use, argamblyopia); hysterical, simulated, and from exhaustion.

Toxic Amblyopia.—The ingestion of or absorption into the system through the lungs, intestinal tract, or skin, of large quantities of certain substances without adequate elimination, or of small quantities in the case of some susceptible organisms, will produce a loss of vision varying in degree from slight up to total blindness. The commonest agents are alcohol and tobacco in combination, lead, quinine, methyl alcohol, Jamaica ginger, coffee, mercury, phosphorus, chloral, opium, ergot, the salicylates, ptomaines. The sight is affected by these substances in several ways—by altering the constituency of the blood and lessening its nutritive value to the ocular structures; by exciting disease of the retinal nerve-cells leading to degeneration of the cells and of the optic-nerve fibers connecting them with the brain-centers and inducing structural changes in the centers for vision. The amblyopia may be acute, as in quinine and methyl alcohol, or chronic, as in tobacco and alcohol poisoning.

The symptoms common to the chronic form are:—

Loss of Vision.—The deterioration is gradual and is usually neglected by the patient until the ability to read is diminished or abolished. Examination shows that vision has fallen to one-half or more for distance and near and is not to be improved by glasses. The patient complains of a bluish-gray smoke or mist constantly before the eyes, and of partial night-blindness. He has no pain and rarely phosphenes or

other signs of irritation of the retina or nerve.

Central scotoma, either relative (colors only) or absolute. Early in the affection, probably contemporaneous with the beginning of the deterioration of vision, the perception for green in the small region of the field controlled by the fovea centralis is lost. Then follows the perception for red and possibly blue. The scotoma may be confined to these colors. Should the disease advance, the scotoma becomes absolute, the perception of all objects being lost in an area of about 10° from the fixation point. The periphery of the field retains its normal dimensions until the onset of optic nerve atrophy, when it undergoes a concentric narrowing.

Papilla Changes.—The ophthalmoscope shows in nearly all instances a whitening of the temporal half of the papilla, with retention of the normal coloring and vascularity of the nasal half. The retina and choroid are unchanged. Even the macula, the point of the fundus which is symptomatically most involved, appears healthy. In about one-third of the cases the optic disk is slightly hyperemic early in the disease and the vessels on the disk are veiled, reflecting the earliest signs of optic neuritis.

Acute poisoning from absorption of methyl alcohol, quinine, pure spirits, etc., causes sudden and complete blindness, even to the loss of perception of light. The action of the poison may be sudden or cumulative. A man of 35 was exposed by the nature of his occupation to the fumes of varnish. He absorbed them through the lungs and the skin of the hands and arms. Feeling in his usual good health when he went to bed, he was awakened several hours later by some cause unconnected with his eyes and discovered he was totally blind. Examination of his eyes the following day disclosed excessive anemia of the disks. The arteries and veins of the retina were invisible a short distance from the nerve-head. A boy of 19 drank an unknown quantity of "white whisky" (95 per cent. alcohol). He was blind the next morning and, except for the temporary return of perception of light lasting a few days, remained blind. The ophthalmoscopic appearances were similar to those in the former case. The prominent symptoms of acute toxic amblyopia are illustrated by both cases: Sudden and complete blindness, partial temporary recovery, ischemia followed by atrophy of the optic nerves and retinas, and permanent blindness.

Amblyopia from Intracranial Causes.—In the preceding paragraph the morbid processes are presumed to be limited to the nervous mechanism of the eye, lying anterior to the chiasm or, if they invade the cerebral tissues, the involvement is secondary and may be considered as a complication. In the intracranial amblyopias the original lesion is cerebral, the secondary in the optic nerves and retina. Uremia of Bright's disease, of pregnancy, and of scarlet fever is a common cause. The amblyopia is usually binocular, rapid in its course, and leads often to complete, but temporary blindness. The prognosis is good. No changes in the eye-grounds commensurate with the degree of loss of vision are to be seen. The retinal veins are distended, dark, and tortuous, and the edges of the disk veiled by edema of the nerve and adjacent retina. The cerebral vessels present a similar condition, namely, reduced supply of

arterial blood, venous stagnation, and diffused serous exudation into the brain substance. The foreign elements contained in the blood doubtless are a contributing cause to the disturbed brain functions. With the establishment of free secretion of urine or artificially induced active diaphoresis the poison is eliminated from the blood, the serum absorbed, and the vision and cerebration restored; or, the kidneys refuse to act, the skin cannot be stimulated, and death ensues.

Rarer forms of amblyopia due to obscure intracranial lesions are the "crossed" and the "hemianopsias." Mills says (Posey and Spiller): "As the fibers of the macular bundles are undoubtedly distributed to the pregeniculatum, complete destruction of this body, or of a special portion of it, would cause central amblyopia of the crossed variety." In the hemianopic variety one-half of the macular field is lost and the other half preserved. Thus one-half of a word or other small object close to the eyes is obscured and can be seen only by movement of the ball. In explanation Mills further says: "A strictly limited lesion of the calcarine cortex on the one hand and of the angular region on the other may cause blindness in half of the macular field of the corresponding sides."

Hysterical Amblyopia.—The features characteristic of this affection are partial or complete blindness, monocular or binocular, without discoverable changes in the ocular structures or signs in the eye or elsewhere in the body of organic disease of the brain or nervous system. The loss of vision may arise spontaneously, or appear at the termination of an attack of general hysteria, or be due to a slight traumatism to the eye or head. The traumatism is, as a rule, slight and out of all proportion to the seriousness of the subsequent complaints. Amblyopia may be the only ocular symptom or it may be complicated by ptosis, recession of the near-point, pupillary inequalities, or disturbances in the field of vision. The alteration in the size and form of the field presents three possible features: concentric contraction, which is not in the least characteristic of hysteria; reversal of the normal limits of the color fields, and the tubular field. Traumatic cases recover promptly and wholly after the cause, for instance a suit for damages, is removed. Cases of spontaneous origin and those dependent upon functional derangements of the nervous system are more persistent, often recur, continue weeks and months, and recover only upon the restoration to health of the individual. It must not be forgotten that blindness without ophthalmoscopic findings or evidence of disease of the cerebrospinal system may not always be diagnosed as hysterical, and that it may have an organic cause to become manifest in time. To make the diagnosis positive it should be associated with at least some of the well-known stigmata of hysteria.

Simulated Amblyopia.—The differential diagnosis between simulated and hysterical amblyopia is rendered difficult by the similarity of the two affections and because both occur in the same class of patients, the neurotic and those of hypersensitive organizations. Pretended, feigned, or simulated blindness is found among recruits for the army and navy services, those who wish to escape positions in which danger or punishment may be incurred, and those who wish to create false impressions and exaggerated estimates of their

physical disabilities, especially in lawsuits for damages. Simulated amblyopia of both eyes is rare and detection difficult. Reliance must be placed on the action of the pupils and the want of relation between the apparently normal eyes and the symptoms. The monocular form, however, may be, as a rule, easily detected. The ophthalmoscope shows clear media and healthy eye-grounds; a strong spherical lens placed before the sound eye will prevent accurate vision in that eye beyond the focal distance of the glass; a prism of 5°, base down or up, will give vertical diplopia; a prism of 10°, base out, will cause a manifest rotation of the eye inward, unconsciously made to fuse the horizontally induced double images; a lead pencil placed before the sound eye will not interrupt reading; the pupils respond to light and convergence almost uniformly. The tests will more successfully deceive the patient into admitting visual power in the assumed blind eye if his attention is directed by them to the sound eye. Radiography is also valuable in the diagnosis. An individual may claim that the blind eye contains a fragment of glass or other foreign material impervious to the rays. In such cases a shadow is cast on the plate when the claim is true. In trolley accidents it frequently happens that the glass of the doors or windows is shattered and the hysterical or fraudulently inclined passenger asserts that he was blinded by the entry and retention in his eye of glass. Examination with the ophthalmoscope cannot invariably exclude the presence of the foreign body, particularly when it has lodged in the ciliary region or when the media are clouded.

Amblyopia Exanopsia.—*From congenital defects* in the ocular structures, such as cataract, polar and lamellar; coloboma of the lens or uveal tract; persistent pupillary membrane; albinism. Rays of light are obstructed in their passage through the eye by the opaque media, they are not clearly focused on the retina by reason of irregular refraction, or they fall upon insensitive retinas or those unsupported by choroidal pigment. In these cases it is probable that early in life the retinal centers in the brain are active and do not, either by disease or congenital anomaly, contribute to the blindness. The cataracts may be removed and vision restored when the operations are performed at an early age. Later, when the brain-centers have been trained and the habits of special sense perception have been formed, operations, although surgically successful, do not materially improve vision.

From Defects of Refraction.—In grades of hyperopia from 2 D. to 5 D. in childhood, binocular vision may early become unattainable. The child unconsciously, in order to obtain good vision, makes extraordinary claims on the accommodation. But the ciliary muscle (accommodation) is supplied by nerve power by the third or motor oculi nerve, which also supplies the muscles of convergence. Therefore, excessive stimulation of accommodation or that surpassing the normal relation between accommodation and convergence compels a proportionately equal degree of convergence. Since both eyes cannot converge simultaneously in distant vision, one eye assumes the abnormal convergence and the other eye is used for fixation. Both eyes retain their normal power of rotation, but each becomes in a sense independent of the other: the one is used for seeing; the other squints. The

former has been the better eye from the beginning, either by reason of less error of refraction or more perceptive retina. The latter gradually becomes amblyopic from disuse. The retina loses its sensibility, the optic nerve its conductility, and the cerebral centers their function. In some children no reason can be assigned for preference of one eye. The error of refraction may be no greater and the rotatory power no less in the squinting than in the fixing eye. Here we must assume that the fault lies in the retina, nerve, or brain. Improvement of vision may be obtained by the forced use of the eye and the compulsory activity of the cerebral center, but vision equal to that of the non-squinting eye is seldom or never acquired unless the usefulness of that eye is destroyed by accident or disease. Habit and the cultivation of the visual apparatus that accrues from habit can not be ignored. Should, however, the treatment for defective vision be instituted very early, before anesthesia of the nervous apparatus of the squinting eye has developed, an appreciable benefit may be gained by the use of the amblyoscope, closure of the fixing eye by bandage, or atropinization of that eye.

Amblyopia from Exhaustion.—Amblyopia in consequence of excessive indulgence in coitus or masturbation has been recorded. It is a purely nervous affection. Upon removal of the cause and the administration of strychnine the cure is generally rapid and complete. Sudden loss of blood in large quantities, occurring sometimes in intestinal ulceration, after delivery of the child in confinement, rupture of blood-vessels by ulceration or accident, may be followed in a few hours by temporary loss of vision. The amblyopia becomes permanent only in cases of degeneration of the ganglion cells of the retina or of the fibers of the optic nerve.

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AMENORRHEA. — DEFINITION.—Absence of the menstrual flow in women of a suitable age who are not pregnant. Suppression of menses, the menstruation having ceased through some local or remote disorder, is also termed amenorrhea.

VARIETIES. — Amenorrhea may be *complete,* when the menstruations will have completely ceased; *comparative,* when it appears occasionally; *primary,* when the menstruation has not presented itself at the age of puberty nor subsequently; *secondary,* when transitory or accidental, or, having already appeared, the menstruation ceases.

SYMPTOMS.—No other symptom than absence of the menstruation may be present, or the monthly flow may be absent and the general attendant phenomena usually preceding menstruation occur. Frequently the patient complains of headache, heat-flashes, fever, nausea and vomiting, and heaviness in the abdomen. Concomitant nervous disorders may form the basis of acute manifestations, hysterical especially. When the amenorrhea is due to obstruction, whether congenital or acquired, the patient does not experience severe pain, but rather a continuous dull aching in the pelvis and over the sacrum, aggravated at the periods when the menstruation should occur by the symptoms above mentioned, known as menstrual molimina.

Pure suppression of the menstruation rarely causes symptoms, espe-

cially when the impending general disorder is the cause of the amenorrhea.

> Case of complete amenorrhea in a Greek woman of abot 40 years with no evidence of defects of any kind, and with good average intelligence, who complained of minor nervous troubles which accompany menopause. The woman never had menstruated; she had given birth to 11 children, 5 of whom were living at time of examination; the grandmother of the patient had never menstruated; the mother of the patient had menstruated only once in every one or two years. Of the patient's children, 1, a girl of 14 years, had not yet menstruated. The patient herself was married at the age of 15 and gave birth to her last child four years ago. Patient further said she had never had symptoms of a menstrual molimen of any sort whatever, no knowledge of when her menstrual time might be due, no malaise, no pain, nothing, in fact, saying that she simply lived like a man and didn't know what it was to be sick. A. R. Hoover and J. K. Marden (Surg., Gynec. and Obstet., March, 1911).

The menstrual flow may be substituted by a profuse leucorrhea which is thick, viscid, and of a yellow or greenish-yellow color. Remote symptoms may present themselves, doubtless of reflex origin.

ETIOLOGY.—The discussion of the causes of amenorrhea is rendered difficult by our want of knowledge of the forces which produce the periodical recurrence of menstruation. Primary amenorrhea is generally due to imperfect or insufficient development. In cold countries the individual matures more gradually and the menstrual flow appears later than in warm countries, where development is rapid, but where, also, women enter stages of decrepitude at an earlier date. Anatomical imperfections and anomalies, the absence of any of the genital organs, or a rudimentary or infantile uterus may thus account for the total absence of menstruation. Imperforate hymen is a frequent, though easily recognized, cause.

Whether we ascribe the periodical occurrence of menstruation to nervous irritation, to the influence on the mucous membrane of the uterus of a superabundance of lime salts in the blood or to the chemical influence through the blood of a secretion of the corpus luteum, the causes of amenorrhea can be divided into four classes:—

Nervous Disorders.—Grief, anxiety, fright, and anger are as many possible primary causes, especially if the patients are poorly fed. According to Bloom, probably not less than 33 per cent. of women emigrants under 30 years of age suffer from suppressed menstruation after a sea-voyage. Many have abdominal distention, and not infrequently girls have been innocently charged with being pregnant. Obstinate constipation is a common symptom. The true etiology is largely psychical and neurotic.

> Series of cases which present certain well-defined clinical features. These prominent characteristics are: (1) diminished or arrested menstruation; (2) local symmetrical imperfect oxygenation of the blood of the extremities, especially the arms and hands—a condition known as "Raynaud's phenomena," and (3) pulmonary tuberculosis. The presence of any single one of these symptoms in patients is observed every day, but attention has not hitherto been called to the remarkable association of all of these clinical features in the same individual. This trilogy of symptoms did not always appear contemporaneously in any of the patients who were affected. In all of them, when first seen, the local asphyxia and the irregularity of menstruation were marked; in two

of the patients pulmonary tuberculosis was also coexistent with the other clinical features mentioned, while in two other patients it developed at a subsequent period. J. W. Byers (Lancet, Aug. 26, 1899).

Case of a young married woman who found that, as soon as she left London and went to the country, her menstruation would return at the regular times, but would not if she remained in town. By leaving town for two days each month it was possible for her to regulate the monthly function. W. J. H. Hepworth (Lancet, Nov. 10, 1900).

The causes of primary amenorrhea at puberty not due to congenital atresia may be distinguished into three varieties, viz.: 1. Cases without discoverable cause, in which the genital organs are apparently perfectly normal. 2. Those due to some congenital defect. 3. Amenorrhea accompanying some general disease, as diabetes or tuberculosis. In the first, local or general treatment may cause appearance of the menses, the prognosis in the other two varieties being unfavorable. The writer cites a case in which menstruation occurred after grafting of a healthy ovary from another subject in the uterine wall. V. le Larier (Paris Thesis; Zentralbl. f. Gynäk., Nu. 35, 1905).

Women who either greatly fear or greatly desire to become pregnant, newly married women, and women who are confined in prisons or insane-asylums furnish a large proportion of the cases. Removal from country to city or *vice versâ,* especially when coupled with nostalgia, is a prolific cause. On general principles, change in the mode of living or of climate, especially with an intervening sea-voyage, appears to frequently act as the etiological factor.

Amenorrhea may be an early symptom of brain tumor and in acromegaly may precede every other symptom by several months and be followed by optic atrophy.

General Affections.—Amenorrhea frequently occurs after a serious illness, such as typhoid fever, eruptive fevers, mumps, pneumonia, or during the course of any chronic disease, diabetes, cancer, malaria, at the onset of severe syphilis. Intoxication of the system, as in morphinism, alcoholism, and hydrargyrism, is also a recognized cause. Syphilis is also thought capable of causing amenorrhea.

Eighteen cases in which the morphine habit caused amenorrhea. It is usually complete and accompanied by loss of sexual desire, but the functions are re-established if the habit be broken. Lutaud (Revue gén. de clin. et de thér., May 2, 1889).

Three cases, aged from 28 to 42, in which amenorrhea persisting from six to eight years was probably due to syphilis. They all exhibited characteristic symptoms of tertiary syphilis, and were subjected to a rigid mercury and iodide treatment which resulted in the return of the menstrual flow. Meirowsky and Frankenstein (Deut. med. Woch., Aug. 4, 1910).

It may be consequent upon an acute or chronic surgical affection, a blow, or injury. Luxurious living and want of exercise, obesity, and excessive intellectual labor at the period of puberty, when not counterbalanced by fresh air and active exercise, may retard the development of the generative organs and thus induce the disorder.

Blood Disorders and Wasting Diseases.—Anemia and idiopathic chlorosis, pernicious anemia, leukemia, and Hodgkin's disease are the most prominent factors. The following causes of waste—and directly, therefore, of amenorrhea—are also to be remembered: Hemorrhage, albuminous discharges; hemorrhage from

piles, scurvy, purpura, and injury, as in hemophilia; hemorrhage from the stomach, as in gastric ulcer; from the lungs, or from the nose, and from a rare disease produced by a parasite in the duodenum: the *Ankylostoma duodenale*. Long-continued suppuration, albuminuria, chronic diarrhea, malignant ulcers, tubercular disease, all impoverish the blood, and so may cause anemia. All diseases that cause wasting of the body finally cause the menstruation to cease. Chief among these are phthisis, diabetes, caries of bone, protracted or febrile illness; anorexia nervosa, the patient wasting because she will not eat; and gastric ulcer.

The occurrence of menstruation is associated with increased vascular tension; hence, any condition which decreases tension will favor amenorrhea.

Lesion of Genitourinary Organs.—Amenorrhea may be associated with any lesion of the genital tract, though less likely to occur in inflammatory conditions. Adhesions from pelvic peritonitis are an occasional cause of hyperinvolutions of the uterus and amenorrhea as a symptom.

> In those cases where the follicular stroma of the ovary has been the seat of an inflammatory process during the infectious fevers, the patient may have an amenorrhea which may remain and become permanent. Alexander Simpson (Practitioner, Aug., 1898).

Atrophy of the ovaries, senile atrophy following pregnancy, and cystic ovarian degeneration are among the less common etiological factors. A most complete examination of the pelvic organs, under ether, if necessary, should be made in such cases.

> If menstruation does not appear at the age of puberty, a careful scrutiny on the part of the physician is obligatory and imperative. Case of a young woman, 24 years of age, in whom the amenorrhea was of organic origin. A dermoid and a suppurating multilocular cyst were found and removed. Report of the pathologist harmonizes with the theory of the case, both from physiological and pathological standpoints: 1. That the dermoid had usurped the place and destroyed the function of the right ovary. 2. In one of the cyst-walls of the multilocular ovarian cyst was found a shrunken ovary the size of a large lima bean, and within this ovarian stroma was found a corpus luteum spurium. To the presence of this ovarian stroma was due the womanly development, with ovulation and the futile effort of menstruation and its consequent suffering. 3. The case demonstrates the possibility of ovulation without menstruation. 4. It leaves doubt whether the absence of the oviducts was primary or secondary to the grave disease of the ovaries, with the possibility that they were congenitally absent. 5. It presents the rare and exceptional condition of a perfectly developed woman who had an ovary and a uterus, who ovulated, was sterile, and never menstruated, and yet was ruined in health by nature's effort to establish an impossible normal function. W. B. Chase (Amer. Jour. of Obstet. and Dis. Women and Children, Oct., 1898).

Exposure to cold during menstruation, by inducing congestion of the pelvic organs, is one of the most active exciting causes, especially when supplemented by a local chronic disorder. The most important condition with which this disorder might be confounded is pregnancy.

> Case of a healthy girl, aged 15, who had been subject for a year to gradual swelling of the abdomen. The period had ceased for two months only. The breasts became hard and tense. The hymen was intact. Peritonitis of tuberculous origin suspected. On opening the abdomen an enormous cyst, which contained twenty pints of fluid, discovered. Its pedicle was twisted and had

risen in the parovarium. On the day after the operation the catamenia reappeared and the abdomen soon resumed its normal form. Cortiquera (Anales de Obst., Gine., y Ped., Jan., 1896).

Case of a young woman who presented many of the usual signs of pregnancy, including cessation of the menses, prominence of the abdomen, etc. On examination deposits of adipose tissue were found in the abdominal walls, while the uterus was small—smaller, indeed, than usual. Subsequent events proved it to be a case in which obesity had led to disturbance, if not, indeed, early appearance, of the menstrual function. Robert A. Reid (Mass. Med. Jour., Aug., 1898).

Case of two girls, 19 and 21 years old, in whom a dense circular band high up in the uterine cavity seemed to obstruct completely the escape of the menstrual fluid. No definite diagnostic features suggested the presence of this unusual condition. In both cases it was accidentally discovered when through a vaginal incision the anterior uterine wall was split longitudinally and the uterine cavity laid open. In both cases the operation was followed by menstrual discharge. Rieck (Münch. med. Woch., March 16, 1909).

PATHOLOGY.—A pathological identity can hardly be attributed to amenorrhea, owing to its complex causes, the diverse physiological conditions peculiar to the cases, and the diathetic conditions that may be present. The fact that the true nature of menstruation itself is unknown adds another objection, and it may safely be said that the pathology of amenorrhea is that of the diseases causing it, until the local disorders brought about by each will have been determined.

DIAGNOSIS.—Primary amenorrhea—that is, total absence of menstruation—is usually due, as already stated, to the absence of one or more of the organs of generation. It must be distinguished from retention of the menses due to atresia of the cervical canal, of the vagina, or of the vulva. In the latter case no menstruation has existed, but the general premonitory symptoms of menstruation have occurred, though followed by no menstrual flow. Cases in which one or more of the organs are absent are not very infrequent, while cases of imperforate hymen are comparatively common.

PROGNOSIS.—Amenorrhea due to absence of any of the organs is, of course, incurable. The same may be said where the approach of the menopause or other conditions point to premature senility of the uterus, which involves the inhibition of the menstrual period. Although amenorrhea, when due to a serious chronic disease, is usually cured with difficulty, hope may always be entertained when the causative disorder is not in itself a fatal one. Return of the menstruation in any chronic disorder, when the blood presents its normal appearance, is an encouraging sign.

TREATMENT.—No woman should be treated for amenorrhea until the possibility of its being caused by pregnancy has been eliminated, if necessary by a careful physical examination. Not infrequently will pregnant women desirous of escaping the responsibilities of maternity seek a consultation with the hope that some drug shall be administered or instrument inserted which will terminate the condition.

Amenorrhea should always arouse concern; it may be the first symptom of acromegaly, to which it stands in about the same relation as ordinary goiter does to exophthalmic goiter, the hypophysis cerebri being so often in-

volved. The amenorrheic should take special pains to avoid chilling, especially of the feet, and every catarrhal affection should be treated with great care. Three such patients in the writer's practice had previous sinusitis, commencing in 1 case at the time the menses became irregular. Special care should also be paid to treatment of syphilis in this connection; it may be injuring the hypophysis even when there are no apparent manifestations elsewhere. His experience further indicates that a pregnancy is liable to aggravate disease of the pituitary body. He discusses the points in which morbid amenorrhea resembles and differs from natural amenorrhea in pregnancy and after the menopause. Acromegaly is the form of amenorrhea in which there is sugar in the blood in almost half of the cases, and there is hypertrophy of the bones of the face. Rosenberger (Zentralbl. f. innere Med., Feb. 25, 1911).

It should be kept in mind that amenorrhea is a symptom, and its cause be diligently sought as a preliminary measure to treatment. Drugs which are considered to exert an influence in promoting the menstrual flow are known as emmenagogues, and are divided into two classes, medicinal and physiological.

Severe physical shock or fright sometimes causes the menstruation to return suddenly.

When the arrest of menstruation is due to exposure to cold, **warm baths** and **vaginal injections, sinapisms** to the thighs and calves of the legs, **saline laxative** and **manganese-binoxide** pills (2 grains each), 1 or 2 after each meal, are frequently successful. This drug acts by increasing the vascularity of the pelvic organs. The **permanganate of potassium**, or the **lactate**, in 1-grain doses three or four times daily, after meals, act in the same manner.

Potassium permanganate may be given daily until the catamenia appear and complete their course, when the salt should be discontinued; it should be recommended four days before the access of the next period, and continued until the flow ceases. It is useful in girls who, on leaving the country and coming to town, suffer from arrested menstruation; also in the amenorrhea induced by seasickness and in the case of women, between 30 and 40, generally married, who while rapidly increasing in weight suffer from a diminished menstruation. Potassium permanganate is given up to 1, 2, or more grains in pill form thrice daily, after meals. The pills should be made after the following formula: **Potassium permanganate**, gr. j; **kaolin and petroleum cerate**, in equal parts, q. s. Certain observers deny that the permanganate produces abortion, but some cases of abortion apparently due to the drug have been observed. (Practitioner, Feb., 1911).

In the amenorrhea following seavoyages the preparations of **manganese** and **oxalic acid** hold the first place.

When the manganese preparations fail, **santonin**, 10-grain doses at bedtime, is especially valuable in chlorotic subjects.

The general system should be invigorated by attention to diet, sleep, and clothing. **Out-of-door life, light exercise,** and **sunlight** are most important. This is especially the case when there is rapidly increasing obesity. In the latter case the **diet** should be regulated, **saline laxatives** administered, or a cure at **Marienbad** recommended. The administration of **thyroid extract** is especially effective in premature menopause from obesity, and should be associated with **active exercise.** Stimulation of the ovaries and uterus by the **faradic current** is especially efficient in such cases.

Cupping or **scarifying the cervix** is sometimes successful. These means

increase the pelvic congestion and tend to counteract uterine or ovarian torpidity.

Rudimentary organs or atrophy of the uterus, if not too great, should be treated by **dilatation of the uterus** with tents and stimulated by the faradic current. The introduction of a **stem pessary** which is to be worn for a number of months not infrequently increases the growth of a rudimentary organ and establishes the function of menstruation. **Exercise** and **nourishing food** should also be given. **Sea-bathing** is of assistance in such cases.

> The **stem pessary** yielded excellent results in the writer's hands in the treatment of the following special types of primary and secondary amenorrhea: 1. In the small, narrow infantile uterus in otherwise well-developed girls. 2. In a class of cases in which menstruation has been regular and normal for years, but at the age of 30 or 35 becomes scanty and skips, and is painful in unmarried women who take little exercise, but work hard mentally. The uterus undergoes premature atrophy and is found small. 3. In women who live high, have good digestion, and become fleshy, the menstruation becomes scant and sometimes disappears entirely. J. H. Carstens (Jour. Amer. Med. Assoc., Nov. 20, 1909).

The rheumatic diathesis occasionally plays a part as an etiological factor. In such cases the **ammoniated tincture of guaiac**, 1 dram in milk three times a day, or the **tincture of colchicum root**, 10 drops every three hours until the bowels become free, will sometimes restore arrested menstruation. The **salicylate of sodium** is also valuable in this connection. **Apiol**, 4 grains daily in 1-grain pills, for fifteen days, has given good results. **Fuchsin** has been highly recommended as an effective drug in re-establishing the menstrual flow.

> Two cases in which amenorrhea was due to pressure upon the uterus, in 1 case by a cyst, in the other by a hematosalpinx. Removal of these obstructions was followed by regular menstruation. Rieck (Münch. med. Woch., March 16, 1909).

Electricity is of great value, faradism, static electricity, galvanism, and galvanic intra-uterine pessaries being applicable according to the nature of the case.

Extract of cows' ovaries has been used with success, but further trials with this agent are required to establish its actual value (see ANIMAL EXTRACTS: Ovarian Organotherapy).

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AMIDOACETPHENETIDIN HYDROCHLORIDE. See PHENOCOLL HYDROCHLORIDE.

AMINOFORM. See HEXAMETHYLENAMINE.

AMMONIA. — Ammonia, chemically NH_3, is made in large quantities from coal gas by heating the ammoniacal liquor with calcium hydroxide, thus conducting the gas formed through tubes containing charcoal. It may be conveniently obtained in smaller amount by heating an ammonium salt, such as ammonium chloride, with dry caustic soda (sodium hydroxide) or slaked lime (calcium hydroxide). It can be formed by the direct union of nitrogen and hydrogen under the electric spark, and is widely produced in nature through the putrefaction of albuminous substances.

PROPERTIES.—Ammonia is a transparent, colorless gas, having an extremely pungent odor and acrid taste. It is strongly alkaline in reaction, and

dissolves very readily (to the extent of 700 volumes) in water, forming a strong solution designated as ammonium hydroxide (sp. gr., 0.897 at 25° C., U. S. P.).

PREPARATIONS AND DOSE.—The preparations of ammonia included in the U. S. Pharmacopœia are as follows:—

Aqua ammoniæ (ammonia water, hartshorn), containing 10 per cent. by weight of ammonia gas; dose, 10 to 30 minims (0.6 to 2.0 c.c.).

Aqua ammoniæ fortior (stronger ammonia water), containing 28 per cent. by weight of ammonia gas; used chiefly externally as a vesicant.

Spiritus ammoniæ (spirit of ammonia), an alcoholic solution, containing 10 per cent. of ammonia; dose, 10 to 30 minims (0.6 to 2.0 c.c.).

Spiritus ammoniæ aromaticus (aromatic spirit of ammonia), composed of ammonium carbonate, 34 parts by weight; ammonia water, 90 parts by volume; oil of lemon, 10 parts; oils of lavender flowers and of nutmeg, of each, 1 part; alcohol, 700 parts; water, enough to make 1000 parts. A nearly colorless liquid when fresh, but gradually becoming darker; dose, 30 to 60 minims (2.0 to 4.0 c.c.).

Linimentum ammoniæ (ammonia liniment), composed of ammonia water, 350 parts by volume; alcohol, 50 parts; cottonseed oil, 570 parts; oleic acid, 30 parts. Should be freshly prepared when wanted.

The following non-official preparations have also occasionally been used:—

Fetid spirit of ammonia, composed of asafetida, 1 part; spirit of ammonia, 21 parts; dose, 30 minims (2.0 c.c.).

Camphorated ammonia liniment, composed of ammonia water, 30 parts; camphor liniment, 70 parts.

Ointment of ammonia, composed of ammonia water, 17 parts; lard, 32 parts; oil of sweet almonds, 2 parts.

MODES OF ADMINISTRATION.—Ammonia is miscible in all proportions with water and alcohol. The most agreeable preparation for internal use is the aromatic spirit, which should always be given well diluted with water. As a stimulating inhalation, the gas arising from ammonium carbonate (the ordinary "smelling salts") is frequently employed; but this may readily be replaced by the simple ammonia water, or, if additional care is used, by the stronger ammonia water. The spirit and the water of ammonia have also been administered hypodermically, or even intravenously, as stimulants, though their action is but fleeting, and considerable local irritation may arise. In pneumonia and other dyspneic states a little ammonia water dropped into boiling water at frequent intervals will "soften" the atmosphere and greatly facilitate breathing.

Externally, the stronger ammonia water may be applied in full strength as a vesicant, and the area under treatment should be covered with a watch-glass to prevent evaporation. For counterirritant effects, a 10 per cent. aqueous preparation, such as the weaker ammonia water, or a stronger oily preparation, such as the official ammonia liniment, is suitable. In children with delicate skins these preparations should be further diluted. In spasmodic croup a little ammonia added to water and applied to the child's neck and chest by means of a cloth will often bring considerable relief, though much care is required to have the fluid sufficiently dilute and not to leave it on too long. The evanescence of the effects of ammonia resulting from its volatility requires

that its administration be frequently repeated.

INCOMPATIBLES.—Mineral or vegetable acids and acid salts, which ammonia neutralizes with the formation of neutral salts; salts of the alkaloids, which ammonia may cause to be precipitated by combining with the acid radical (thereby setting free the more or less insoluble pure alkaloid); chlorine, bromine, and iodine, with which ammonia combines to form corresponding salts; mercurial and most other metallic salts, with which ammonia forms insoluble mixed salts or hydroxides.

CONTRAINDICATIONS.—In acute inflammations of the stomach and in cases where the urine is abnormally acid the internal use of ammonia is to be avoided. In small children and in persons with a sensitive respiratory tract, the inhalation of ammonia fumes is likewise apt to be prejudicial, large amounts giving rise to a bronchitis.

PHYSIOLOGICAL ACTION.—**Local Effects.**—Solutions of ammonia strongly irritate any tissues with which they may be brought in contact. Applied to the skin, they act as rubefacients or vesicants, according to the concentration of the preparation used and the length of time it is left on the tissues. On the mucous membranes, especially the conjunctivæ, the buccal and the respiratory mucosæ, ammonia vapor acts primarily as a stimulant, exciting the local nerve-terminals, causing increased flow of glandular secretions, and, when concentrated, spasm of the glottis; when kept in contact for a longer time, ammonia preparations cause inflammatory changes which may result in local death of the tissues, followed by sloughing. The caustic action of ammonia is due, as is the case with other alkalies, to a combination with the tissue albumins, resulting in the formation of alkali albuminates, and with the fats to form soaps. The great penetrating power of ammonia, due to its volatility, renders it, when concentrated, one of the most deeply acting of corrosives.

Effects on Internal Use.—*Nervous System.*—After being absorbed into the circulation, ammonia stimulates, for a short period, the medulla oblongata and the motor side of the spinal cord. The higher brain-centers are, if anything, slightly depressed. The spinal stimulation results in an exaggeration of reflex activity and, with excessive doses, in convulsions. Succeeding the stage of stimulation, a secondary stage of depression of the medullary centers and spinal cord may occur with large doses.

Circulation.—Ammonia stimulates the heart muscle, the vasomotor center in the medulla, and, to a less extent, the inhibitory (vagus) center, likewise in the medulla. These effects result mainly in a pronounced rise of the general blood-pressure. The heart beats more strongly, but its rate is frequently slowed. Excessive doses may lead to a secondary depression of both the heart and vasomotor mechanism.

Respiration.—The respiratory centers in the medulla are strongly stimulated by ammonia. Both rate and depth of breathing are increased through its action.

Secretions.—Ammonia and the ammonium compounds stimulate the flow of body secretions, especially the sweat, saliva, and mucous secretions. The diaphoretic effect is believed to be wholly central, *i.e.*, due exclusively to excitation of the sweat-center in the medulla. The other secretory effects are ascribed both to a central action and to a local effect on the gland-cells.

Digestive Tract.—Moderate doses of ammonia stimulate, like other alkalies, the gastric glands if taken before meals. After meals they neutralize the acids of the gastric juice. Large amounts of ammonia exert a corrosive action on the mucosæ (*v.* Ammonia Poisoning).

Absorption and Elimination.—Concerning the manner in which ammonia exerts its stimulating effect, there are still differences of opinion. Some claim that, after being rapidly absorbed, ammonia, circulating with the blood, stimulates the vital centers directly; others believe that the centers are stimulated mainly reflexly, as a result of the local irritation produced in the stomach.

The researches of Magnus showed ammonia to be neither absorbed nor excreted by the lungs. Hence, in so far as its administration by inhalation is concerned, the stimulating effects of ammonia would appear to be due largely to peripheral sensory stimulation.

When taken internally, on the other hand, ammonia is readily absorbed; but on reaching the blood-stream it rapidly undergoes a chemical change whereby it is converted into the relatively inert substance urea. Whatever direct stimulating action it may exert on the nerve-centers and heart is, therefore, quickly brought to an end.

By the conversion into urea, the ammonium in ammonium hydroxide loses the characteristics of an alkali metal. For this reason ammonia does not increase the alkalinity of the body fluids, differing thus from the hydroxides of sodium and potassium, which cannot undergo the change referred to.

The urea produced from the ammonia is naturally eliminated largely with the urine, which may be somewhat increased in amount owing to stimulation of the renal cells by the excess of urea.

TOXICOLOGY.—The ingestion of strong solutions of ammonia results in corrosion or violent inflammation of the mucous membranes of the mouth, esophagus, and stomach, and in marked irritation of the larynx and trachea, owing to the penetration of ammonia vapor into the respiratory passages. The symptoms consist of violent pain in the mouth, throat, and abdomen; salivation; vomiting, sometimes bloody, and, occasionally, purging. The intense irritation of the respiratory mucous membranes may cause, at first, a momentary arrest of breathing and depressed heart action, as well as spasmodic contraction of the laryngeal and bronchial muscles. Later, the persisting laryngeal irritation causes intense local burning and a characteristic difficulty of respiration, due to actual edematous swelling of the glottis. Sudden death by asphyxia may result, though more frequently it is due to shock arising from the pronounced local destructive effects of the alkali, or to collapse, possibly owing to a secondary depressive effect of the drug on the heart and medullary centers. Convulsions, however, are comparatively infrequent in ammonia poisoning, and this fact would tend to indicate that in the majority of cases the amount of ammonia absorbed is insufficient to cause violent direct effects on the nerve-centers.

The ultimate results in cases of ammonia poisoning can seldom be predicted with certainty. Not only may laryngeal or bronchial inflammation follow, but the gastric mucosa may be so greatly injured as permanently to impair the functions of the stomach, and even cause death from inanition. Moreover, in cases that recover from the acute effects, stricture of the esophagus is a frequent sequela. As with other

caustics, the upper and lower extremities of the gullet and the point at which it crosses the left bronchus are the favorite seats of corrosion.

Large doses of ammonia (providing a sufficient amount is absorbed) are said to diminish the oxygen-absorbing power of the red blood-corpuscles and to interfere with coagulation.

Treatment of Ammonia Poisoning.—The chief ends to be sought in the treatment of the first stage of the poisoning are neutralization, dilution, and removal of the obnoxious agent. **Vinegar, lemon juice,** or any other available acid (preferably a vegetable acid), well diluted, should be given, together with a large amount of water. Where no acid is at hand, an oil, such as **olive oil** or **linseed oil,** forms the best substitute. The **stomach-pump** may then be cautiously used, though, if sufficient time for marked corrosion of the tissues has already elapsed, its passage is attended with some danger, owing to the liability of the weakened tissues to perforation.

Morphine should be given if the pain is severe, and **tracheotomy** may be required if asphyxia threatens.

If symptoms of shock or secondary collapse appear, the usual measures for combating these states — hypodermic injections of **ether, digitalis, atropine, strychnine; hot, strong coffee** by the rectum; **external heat, artificial respiration,** etc.— should be availed of.

Demulcents, such as **olive oil, starch paste, tragacanth mucilage, milk, white of egg,** or an **infusion of elm bark,** should be freely administered to soothe the inflamed mucous membranes. No food is to be given by the mouth for two days after the accident.

Strictures of the esophagus should be treated by **dilatation with bougies** (*v.* Esophagus, Stricture of).

APPLIED THERAPEUTICS OF AMMONIA.—As a Stimulant.—Ammonia is of great value as a rapidly acting "diffusible" stimulant, exerting a marked beneficial effect in all forms of **acute circulatory, respiratory,** and **nervous depression.** It may be administered either by the mouth, by inhalation, or by hypodermic or intravenous injection. For internal use, the aromatic spirit of ammonia, always well diluted, in doses of 15 minims to 1 dram (1 to 4 c.c.), is the best preparation. For inhalation, ordinary ammonia water, or "smelling salts," may be used. The effect of ammonia, when it is taken internally, is believed by some to be chiefly reflex, varying in intensity with the degree of local irritation produced. A similar mode of action is known to obtain when ammonia is inhaled; none of it is absorbed through the lungs, and the effect is correspondingly fugacious. The true stimulating effect of ammonia is best obtained by intravenous injection, though the hypodermic method is oftener employed.

In **asphyxia,** whatever be its origin, ammonia is a valuable agent. It may, with advantage, be given at once internally and by inhalation. During the latter procedure care should be taken not to spill any of the strong liquid into the patient's mouth or nose,—an accident which is likely to occur when the patient is recumbent, and which is apt to yield a more pronounced effect, however, than its ingestion.

In cases of **sudden heart-failure** or **collapse,** as may result from the presence of bacterial toxins or poisoning by depressant drugs, such as hydrocyanic acid, chloroform, chloral hy-

drate, aconite, etc., repeated ingestion of 15 minims to 1 dram of the aromatic spirit of ammonia, diluted with half a tumblerful of water, or the intravenous injection of like amounts of ammonia water, diluted with 6 drams of sterile water, will usually exert a powerful stimulating action. Ammonia may likewise be used internally to combat the effects of **bites of poisonous animals.**

In ordinary "**fainting**" and the lighter forms of **shock**, the inhalation of ammonia from its solution or from smelling salts may suffice to bring about the desired result.

In infants, collapse occurring in **summer diarrhea** may be combated with occasional doses of a few drops of ammonia, well diluted.

For the algid stage of **cholera**, ammonia internally and ether hypodermically, with simultaneous free administration of alcohol, have been highly recommended by Giacich. Marked improvement in the general condition was noted within two hours after the institution of this mode of treatment, and over 50 per cent. of cases already in the algid stage are said to have recovered.

In **acute alcoholic intoxication**, the ammonia preparations are considerably used. Lavage of the stomach, followed by the administration of 10 drops of ammonia water in a half-tumblerful of water, will often counteract promptly the effects of the alcohol. Ammonia has also been used with benefit in the treatment of **delirium tremens** (Butler).

As an Antacid.—Internally, ammonia may be used to counteract **gastric hyperacidity**, indicated by such symptoms as acid eructations ("heartburn") and flatulence. Particularly where there are pronounced abnormal fermentative processes, resulting in the formation of vegetable acids, does ammonia appear to be efficient. A few drops (3 to 5) of the water of ammonia, or 10 drops of the aromatic spirit, well diluted, will often give relief under these circumstances. It should be remembered that, although the ammonia introduced will tend to neutralize any acids present, the local irritation produced by it will, in addition, tend to stimulate the gastric glands and musculature. Hence the special degree of benefit obtained where there is **flatulence** and in cases where the gastric functions are weakened by **general debility** or **excessive alcoholic indulgence.**

In **poisoning by mineral acids**, such as hydrochloric or sulphuric acids, well-diluted ammonia may be given as an antidote (though a less-irritating alkali, when at hand, is much preferable).

Externally, in painful **insect bites**, ammonia may be used to neutralize the acid (frequently formic acid) introduced at the moment of stinging. Its antiseptic action is also helpful.

As a Counterirritant, Rubefacient, or Cauterant.—Ammonia water applied to the skin acts powerfully in relieving subjacent pain, though the superficial pain attending its use is not infrequently more severe than is the case with other counterirritants.

In patients with kidney affections, in particular, it has been used as a vesicant in place of cantharides, which causes harmful renal irritation in these cases. It has the property of passing through the horny layer of the epidermis without destroying it (as would other strong alkalies), and of inducing blister formation through irritation of the dermis.

In **bruises, chilblains,** and other superficial lesions, ammonia liniment may be employed as a rubefacient. It sometimes relieves the milder forms of **chronic rheumatism,** including the joint manifestations and **lumbago.**

The corrosive and antiseptic properties of ammonia may be utilized with great advantage and convenience in treating the **bites of carnivorous animals, venomous reptiles and insects.** In snake-bites, for example, strong ammonia water may be applied directly to the wound, the general stimulating effect of ammonia being also availed of by giving an intravenous injection of 30 to 60 minims of the weaker solution in 6 drams of sterile water. In insect stings, the local application of ammonia water will often greatly reduce the pain or itching; especially where a tendency to local infection exists, the antiseptic property of the remedy may be utilized with great benefit. The patient should always be cautioned, however, to remove the ammonia when marked redness of the skin appears; otherwise, considerable local injury is likely to result. In a case witnessed by the writers, the patient had used it in the form of a compress to treat a horse-fly bite. The large area thus "treated" resembled a burn of the second degree. Most people handle ammonia carelessly.

In the "hair tonics" recommended in premature **alopecia,** ammonia water is considered a valuable ingredient. The aromatic spirit of ammonia is also used in various other affections of the scalp, including **pityriasis,** etc.

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AMMONIUM.—A metal-like body, never yet isolated in pure form, but known, from the manner in which its compounds can be formed by the interaction of ammonia gas and acids, to have the chemical composition NH_4. The compounds of ammonium greatly resemble those of potassium; hence the inclusion of ammonium in the group of alkali metals. The official salts of ammonium are the following:—

Ammonii benzoas (ammonium benzoate); dose, 5 to 30 grains (0.3 to 2.0 grams).

Ammonii bromidum (ammonium bromide); dose, 5 to 30 grains (0.3 to 2.0 grams).

Ammonii carbonas (ammonium carbonate); dose, 2 to 15 grains (0.12 to 1.0 gram).

Ammonii chloridum (ammonium chloride); dose, 2 to 30 grains (0.12 to 2.0 grams).

Ammonii iodidum (ammonium iodide); dose, 3 to 15 grains (0.2 to 1.0 gram).

Ammonii salicylas (ammonium salicylate); dose, 3 to 15 grains (0.2 to 1.0 gram).

Ammonii valeras (ammonium valerianate or valerate); dose, 2 to 10 grains (0.12 to 0.6 gram).

Ammonium acetate is official in *liquor ammonii acetatis* (spirit of Mindererus), a solution of diluted acetic acid nearly saturated with ammonium carbonate; dose, 4 fluidrams (16 c.c., containing about 15 grains or 1 gram of ammonium acetate), and in *liquor ferri et ammonii acetatis* (Basham's mixture), which is made up of tincture of ferric chloride, 1 fluidram (4 c.c.); diluted acetic acid, 1½ fluidrams (6 c.c.); solution of ammonium acetate, 12½ fluidrams (50 c.c.); aromatic elixir, 3 fluidrams

(12 c.c.); glycerin, 3 fluidrams (12 c.c.), and water, enough to make 25 fluidrams (100 c.c.); dose, 4 fluidrams (16 c.c.).

PHYSIOLOGICAL ACTION.—The effects of the compounds of ammonium are a composite of those of the ammonium group or ion itself, and of the acid group in union with it. The latter may not only modify that of the ammonium, as in ammonium bromide, but may completely overshadow it, as in ammonium arsenate.

The effects of the ammonium ion, when it enters the circulation, are, in general, those of a promptly acting, but fleeting stimulant. If the amount introduced be excessive, depression may follow the primary stimulation.

In the *nervous system* the stimulating effects of ammonium bear chiefly upon the spinal cord and medulla. The motor spinal centers are excited to increased activity, exaggerated reflex action, and even convulsions, being among the most evident results. The cerebrum, however, is, if anything, depressed rather than stimulated. The *circulation* is influenced in various ways: 1. Stimulation of the vasomotor center in the medulla causes a rise of blood-pressure through constriction of the peripheral blood-vessels. 2. The heart muscle is directly stimulated, the result being a strengthening of its beats and further rise in the blood-pressure. 3. Excitation of the vagus (inhibitory) center in the medulla may cause some slowing in the heart rate. *Respiration* is accelerated and deepened through stimulation of the medullary centers presiding over this function. The *body secretions,* especially the sweat, saliva, and mucous secretions of the alimentary and respiratory tracts, are increased by ammonium, partly through stimulation of the nervous centers governing secretory processes (exclusively so in case of the sweat secretion), and partly owing to local effects on the secreting cells.

Though most of the ammonium compounds are readily and promptly absorbed from the stomach and intestines, their excretion through the urine and other secreted fluids is so rapid as to greatly limit the power and duration of their effects when taken by the mouth. Further, certain of the salts of ammonium, *i.e.,* the acetate and citrate, when absorbed, are oxidized to ammonium carbonate in the system, and this, in turn, undergoes a rapid decomposition, probably mainly in the liver, whereby it is converted into urea. The ammonium group is thus destroyed, and its specific effects promptly disappear. Only by intravenous injection of rather considerable amounts of ammonium salts are the effects of the NH_4 group obtained with any degree of intensity.

The decomposition of the NH_4 group into urea involves loss of the alkaline properties of its compounds. For this reason the alkalinity of the blood is not increased and the acidity of the urine not diminished by the administration of alkaline salts of ammonium, as they would be by giving alkaline salts of sodium and potassium.

Ammonium salts which are not changed to the carbonate and eliminated as urea—*e.g.,* ammonium chloride—are excreted as neutral salts, and, therefore, also fail to influence the reaction of the urine.

The contrast between the stimulating action of ammonium hydroxide (ammonia) or ammonium carbonate and the almost complete absence of it in the case of ammonium chloride is now be-

lieved to be due not to any greater rapidity of absorption or more prolonged persistence of ammonium in the blood (the reverse being, in reality, the case), but to the reflex stimulation caused by the caustic alkaline action of the first-mentioned two compounds on the gastric mucosa (or wherever else brought into relation with the organism), as compared to the low degree of local irritation caused by the practically neutral chloride of ammonium.

As already mentioned, some of the ammonium compounds owe their therapeutic value chiefly to the acid group—benzoate, bromide, salicylate, etc.—with which the ammonium is in combination. For information concerning these the reader is referred to the headings under which the respective acids are considered: **Benzoic acid, bromides, salicylic acid,** etc. The more important of the compounds in the physiological action of which the ammonium group plays the leading part will be treated of in the following sections.

AMMONIUM ACETATE.—Ammonium acetate ($CH_3.COONH_4$) occurs as a white crystalline solid, freely soluble in water. It is seldom used in its natural state, but enters into the composition of the official *liquor ammonii acetatis* (spirit of mindererus), which is extensively employed. This fluid is prepared by neutralizing dilute acetic acid with ammonium carbonate (5 grams of the former in 100 c.c. of the latter, according to pharmacopeial directions), the result being a colorless liquid, which may give off a faint odor of acetic acid, and has a mildly saline, acidulous taste and an acid reaction. The preparation is required to contain not less than 7 per cent. of ammonium acetate, and should be freshly prepared when wanted. The dose of spirit of mindererus is 2 fluidrams to 1 ounce (8.0 to 30.0 c.c.), repeated every two or three hours.

Liquor ferri et ammonii acetatis (Basham's mixture) will be considered among the preparations of iron.

MODE OF ADMINISTRATION.—Liquor ammonii acetatis is best administered well diluted in sweetened water. Sparkling water (charged with carbon dioxide) is also advantageous as a diluent.

INCOMPATIBLES.—Strong acids, which enter in combination with the ammonium, replacing the weaker acetate radical; compounds of bases stronger than ammonium (sodium, potassium), with acids weaker than acetic acid, *e.g.,* the carbonates of sodium and potassium; lime water (calcium hydroxide); metallic salts, such as those of silver and lead.

PHYSIOLOGICAL ACTION.—Ammonium acetate, especially when given in the official solution, is the most strongly *diaphoretic* of the salts of ammonium. Its action is believed to take place largely, if not solely, through stimulation of the sweat-center. The diaphoresis occurring under its influence is greatly assisted if the cutaneous vessels are already in a state of dilatation or are caused to dilate by the application of warmth—blankets—to the patient's skin, or by combination with sweet spirit of niter or aconite.

A second useful property of this salt is its action as a *diuretic.* This action is exerted most strongly when diaphoresis is held in abeyance, *i.e.,* when the skin vessels are not dilated. The diuretic effect of ammonium acetate is not produced through irritation of the kidney-cells. This is one of the ammonium salts which are rapidly con-

verted in the system, first into ammonium carbonate, then into urea; hence the diuretic effect is probably chiefly that of urea,—a normal stimulant to the renal function.

Ammonium acetate is believed to be one of the most rapidly absorbed of the ammonium salts; we should, therefore, expect that some of the stimulating action of ammonium on the medullary nerve-centers and circulation would be exerted on ingestion of this salt. Such stimulation does not, however, with the exception of the sweat-center, appear to occur to any marked extent. The reason for the special preponderance of diaphoresis in the action of this salt of ammonium is not definitely known.

THERAPEUTICS.—As a Diaphoretic and Diuretic.—The solution of ammonium acetate is useful as a mild sweat-producer and diuretic in febrile diseases, including **acute coryza, influenza, mumps,** the **eruptive diseases of childhood,** etc. The elimination of toxic products, in which the skin, as well as the kidneys, plays so important a part in these affections, is hastened by it. It also tends to reduce excessive temperatures by increasing the amount of fluid evaporated from the skin. In the diseases of childhood, when the eruption is delayed, ammonium acetate will favor its appearance. It has also been found serviceable in **muscular rheumatism** (Butler).

In **acute alcoholic intoxication** ammonium acetate has been found to remove promptly the symptoms. In **migraine,** too, through some obscure mode of action, and in **amenorrhea,** the remedy has sometimes proved beneficial (Butler).

Externally, solutions of ammonium acetate have been applied as a lotion over **contusions, beginning abscesses** and **glandular enlargements,** and certain skin diseases, *e.g.,* **prurigo.** In **chronic ophthalmic inflammations,** also, it has been used as an eye-wash, a little laudanum being added to the acetate solution in order to relieve local discomfort.

AMMONIUM CARBONATE.—The substance used under this name is not the pure carbonate of ammonium, $(NH_4)_2CO_3$, but is a mixture in variable ratio of acid ammonium bicarbonate, $(NH_4)HCO_3$ or $CO(OH)ONH_4$, and ammonium carbamate, $CO(NH_2)ONH_4$. This mixture is also known as ammonium sesquicarbonate, hartshorn, sal volatile, Preston salts, or bakers' ammonia. It is made by heating an ammonium salt, such as the chloride, with chalk (calcium carbonate), and occurs in white, hard, translucent masses having a sharp, saline taste, a strong odor of ammonia, and a strongly alkaline reaction to litmus. It loses both ammonia gas and carbon dioxide when exposed to the air, and effloresces, becoming opaque and friable. When heated it volatilizes completely. When dissolved in hot water it is decomposed, ammonia and carbon dioxide being driven off; upon further boiling it disappears from the solution by volatilization. It is soluble in 5 parts of water at a temperature of 15° C. (59° F.), and in 4 parts at 25° C. (77° F.). Alcohol dissolves only its carbamate constituent, the acid carbonate remaining. In glycerin it is soluble to the extent of 1 in 5 parts. The purity standard set for ammonium carbonate by the United States Pharmacopœia is that it should contain 97 per cent. of the constituents above mentioned, and should yield not less than 31.58 per cent. of ammonia gas.

The dose of ammonii carbonas is 2 to 15 grains (0.12 to 1.0 gram), the average being 5 grains (0.3 gram).

The aromatic spirit of ammonia (*spiritus ammoniæ aromaticus*), already considered under ammonia (*q.v.*), contains about 4 per cent. of ammonium carbonate.

MODE OF ADMINISTRATION.—Ammonium carbonate should not be given in any form other than a well-diluted solution, thus avoiding excessive gastric irritation and facilitating absorption. The evanescence of the effects of this salt, in common with other ammonium salts, requires that it be frequently repeated, *e.g.*, every two hours. Its unpleasant taste may be covered by licorice.

INCOMPATIBLES.—Ammonium carbonate is incompatible with acids, with acid salts, and with lime water.

PHYSIOLOGICAL ACTION.—Ammonium carbonate possesses, to a certain extent, the stimulating properties of ammonia. As has already been stated, the general stimulant effect of the latter, taken internally, is now believed due not so much to a direct action of the ammonium group on the nerve-centers and circulation after absorption as to the irritation of the gastric mucous membrane due to the strong alkalinity of ammonia. The same view is held with regard to ammonium carbonate, the lesser extent of its stimulating effect corresponding with its lower degree of alkalinity as compared to ammonia. Taken in considerable amounts, the salt causes vomiting.

If ammonium carbonate is injected subcutaneously or intravenously, direct stimulation of the respiratory and vasomotor centers, spinal cord, and heart by the ammonium circulating in the blood (in addition to the reflex stimulation from local irritation, when injected subcutaneously) is produced.

Like the acetate of ammonium, the carbonate acts as a mild diaphoretic and diuretic. It possesses also, to a considerable degree, the property of increasing the bronchial secretions and mucus in general. After absorption it is partly oxidized to urea; but some of it is excreted unchanged by the bronchial and other glands, which are stimulated by it. According to Sollmann, ammonium salts in increasing secretions of the respiratory tract and the saliva act in no less than four ways: 1. By reflex stimulation from the mucous membranes with which the salt is brought in contact. 2. By direct stimulation of the secretory nerve-centers, which the drug reaches through the circulation. 3. By a local stimulating action on the gland-cells themselves, with the secretions of which the salt is excreted. 4. Through liquefaction of the mucous secreted, owing to the alkalinity of the ammonium carbonate eliminated with it. (Several ammonium salts, besides the carbonate itself—the acetate, citrate, etc.—are converted in the system into, and partly eliminated as, the carbonate.)

Ammonium carbonate, like ammonia, is, to a certain extent, antiseptic, owing to its alkalinity. Applied to the skin, it acts as a rubefacient.

The pure neutral carbonate of ammonium—$(NH_4)_2CO_3$—is of physiological importance. The nitrogenous waste product of the activity of muscles is ammonium lactate. This, according to the belief of some, is converted in the tissues into ammonium carbonate, which, in turn, is dehydrated in the liver to ammonium carbonate, and, finally, to urea. Where the hepatic functions are deficient, ammonium car-

bonate or carbamate may persist, and cause symptoms of ammonium poisoning, somewhat resembling those of uremia.

TOXICOLOGY.—Ammonium carbonate, ingested in large amount, brings about nausea and vomiting through local irritation. If brought in contact with the mucous membranes in concentrated form, destructive lesions, somewhat similar to those produced by ammonia, may result. For symptoms and treatment the reader is referred to the section on the toxicology of ammonia.

THERAPEUTICS.—**As an expectorant**, ammonium carbonate is of considerable value. The secretions are both increased and rendered more fluid, being, therefore, removed with greater facility. In **bronchitis, pneumonia, asthma,** and **pulmonary tuberculosis,** the combination of the expectorant effect with the stimulating action on the respiratory centers is very advantageous, more especially in cases where dyspnea is marked. In these affections it should be given in doses of 5 or 10 grains (0.3 to 0.6 gram), repeated every two hours.

In **acute coryza** it may also be employed with satisfactory results.

As a Stimulant.—The stimulating effect of this remedy on the medullary centers and heart is of great value in all conditions of general adynamia, with or without involvement of the respiratory tract. In the **acute exanthemata** of children, and **continued fevers** of various kinds, it may be used with great advantage to sustain circulatory and respiratory activity. In **bronchopneumonia, chronic bronchitis** with marked general weakness, it is a favorite remedy. In **chronic heart disease** with failure of compensation it is also frequently used. The effect is, of course, of brief duration, and frequent administration being required to keep up the action. In **"fainting" (syncope)** and **shock** the inhalation of "smelling salts" (ammonium carbonate reinforced with ammonia water) is a time-honored and effective procedure.

As a Gastric Stimulant or Emetic.—In **indigestion** due to **general weakness,** and in cases where **flatulence** is a prominent symptom, ammonium carbonate may be used to tone up the gastric functions. Its effects are, however, evanescent. In the **indigestion of alcoholics** it has also proven very useful.

Emesis may be obtained by the administration of large doses, *e.g.,* 30 grains (2 grams), of ammonium carbonate. The absence of concomitant depressing effects distinguishes this form of emesis from that caused by depressing drugs, such as tartar emetic.

As a Rubefacient and Discutient.—Ammonium carbonate may be employed as a rubefacient in a manner similar to ammonia (*q.v.*). In **psoriasis,** baths containing ammonium carbonate are given for the purpose of dissolving off the scaly coverings of the lesions, in order that the local remedies subsequently applied may act directly on the skin.

AMMONIUM CHLORIDE, also known as "sal ammoniac" or muriate of ammonia, has the chemical formula NH_4Cl. It may readily be produced by the interaction of ammonia and hydrochloric acid, but is more usually produced by neutralizing ammonia with sulphuric acid, separating by crystallization the ammonium sulphate thus formed, and subliming it with sodium chloride. It occurs as a white, crystalline powder, odorless, but having a cool-

ing, saline taste. In contrast with ammonium carbonate, ammonium chloride is permanent in the air. When strongly heated it is completely volatilized, without decomposition.

Ammonium chloride is soluble in 2 parts of water, in 50 parts of alcohol, and in 5 parts of glycerin at 25° C. (77° F.), and in 1 part of boiling water. Though ammonium chloride is a neutral salt, its solution in water has a slightly acid reaction. This is due to the fact that small amounts of NH_4OH and of HCl are formed in the solution by reaction of NH_4Cl with H_2O, and that the HCl is dissociated into its ions to a greater degree than the NH_4OH, therefore being chemically more active and producing the acid reaction.

The dose of *ammonii chloridum* is 2 to 30 grains (0.12 to 2.0 grams), the average being 7½ grains (0.5 gram). The *trochisci ammonii chloridi* (troches or lozenges), also official, each consist of ammonium chloride, 0.1 gram (1½ grains); extract of glycyrrhiza, 0.2 gram (3 grains); tragacanth, 0.02 gram (⅓ grain); sugar, 0.4 gram (6 grains), with syrup of Tolu, q. s.

MODES OF ADMINISTRATION.—Ammonium chloride is best given in solution or in the form of lozenges. Licorice is decidedly the most advantageous agent for disguising its unpleasant salty taste. The *mistura ammonii chloridi* of the National Formulary, *e.g.*, contains 2½ parts each of the salt and of pure extract of licorice in 100 parts of water. Similarly, the *mistura glycyrrhizæ composita* (brown mixture) of the U. S. P. is often used as a vehicle for ammonium chloride. In affections of the lower respiratory passages inhalations of freshly formed ammonium chloride vapors are also frequently utilized.

INCOMPATIBLES.—Ammonium chloride is incompatible with alkaline compounds or carbonates of the stronger alkali metals,—sodium and potassium,—or of the metals of the alkaline earths,—calcium, strontium, barium; the more strongly basic metals in these compounds tend to displace the ammonium from its chloride. If an ammonium chloride solution to which sodium or potassium hydroxide has been added is heated, gaseous ammonia is evolved. Salts of silver, mercury, or lead, in solution, are precipitated as insoluble chlorides if combined with the chloride of ammonium.

PHYSIOLOGICAL ACTION.—Taken internally, ammonium chloride, being less irritating than ammonia or ammonium carbonate, causes but little reflex irritation of the central nervous system through irritation of the gastric mucosa. In view of the fact, however, that it is destroyed in the blood to a much less extent than ammonium carbonate and ammonium acetate (which, as has already been stated, are largely converted to the relatively inert substance, urea), we would expect ammonium chloride to exhibit the direct stimulating effect of ammonium on the nerve-centers more clearly than the compounds just mentioned. That this is not the case, ammonium chloride being but slightly a general stimulant, tends to support the view, now held by many, that the stimulating effects of ammonium compounds taken internally are exerted through a reflex, rather than a direct, action on the centers. Nevertheless, if the salt be given intravenously, the direct stimulating action of ammonium on the spinal cord, the respiratory, vasomotor, and other centers, as well as the heart muscle, becomes clearly manifest. It may be pre-

ceded by a period of central nervous depression, as was well illustrated in the results obtained by Gourinsky in experiments on frogs and pigeons. His findings were these: In frogs whose spinal cord has been divided below the medulla oblongata ammonium chloride produces, from the first, a marked augmentation of reflex action. In normal frogs and pigeons, on the other hand, ammonium chloride produces, at first, depression of the central nervous system, then convulsions; the higher centers at first exercise an inhibitory influence on the spinal reflexes. When the salt is introduced rapidly, the first stage (that of depression) is but slightly marked, and soon gives place to the second stage (that of irritation, ushered in by convulsions). When it is introduced slowly the depression is well marked and lasts a long time. In frogs and pigeons deprived of the cerebral hemispheres only, whatever be the method of introducing the salt, convulsions are not preceded by depression, but the latter is sometimes replaced by irritability. All the facts, according to Gourinsky, can be explained only by the reciprocal action of the nervous centers on each other, modified by the ammonium chloride. It should be mentioned, in this connection, that, in the frog, ammonium chloride has a tendency to paralyze the motor nerve-terminals in the muscles; in mammals, however, this effect is hardly noticeable, even with large doses.

The most important action of ammonium chloride is that on the secretions of the respiratory passages, stomach, and mucous membranes in general, which are increased and rendered more fluid by it. The several ways in which this effect may be produced have been set forth under ammonium carbonate (*q.v.*). The fact that some of the salt is eliminated by the mucous membranes suggests that the direct action of the drug on the gland-cells must play an important rôle in the effect produced. Its elimination with the sweat and urine also causes it to be mildly diaphoretic and diuretic, as well as expectorant.

Ammonium chloride has been found to produce an increase in all the solids of the urine, except in uric acid.

When given continuously for some time, it is believed to cause pathological alterations in the blood, which may eventuate in general prostration, together with hemorrhage under the skin, from the mucous membranes, and hematuria.

Externally, ammonium chloride, in strong solutions, acts as an irritant.

THERAPEUTICS.—As a Stimulant to Mucous Membranes.—*In Disorders of the Respiratory Tract.*—Ammonium chloride has long been considered an effective remedy in almost every disorder of the respiratory tract. More recently the carbonate has replaced it in the treatment of pulmonary disorders, but the chloride is still widely used in **chronic bronchitis** and **acute bronchitis** after the initial stage of the bronchial inflammation has passed that of marked congestion and dryness. In **whooping-cough**, also, ammonium chloride has given fairly good results. The drug acts, at least in part, directly on the gland-cells of the mucous membranes, with the secretions of which it is eliminated into the bronchi. The cells are stimulated by virtue of its "salt action," the result being a less tenacious and more watery secretion of mucus, which is more readily evacuated. Frequently the drug is given in combination with other stimulating expectorant remedies. In the terminal stage of

acute coryza and in subacute or chronic forms of pharyngitis and laryngitis, the beneficial effects of ammonium chloride on the mucous membranes are also utilized with advantage.

In **pneumonia**, ammonium chloride has been given in 10-grain (0.6 gram) doses every two hours, in the hope of in some way favorably modifying the inflammatory process in the lung, but the results obtained have not been striking (Brunton).

Fumes of nascent ammonium chloride, generated by the action of hydrochloric acid on ammonia, are frequently administered by inhalation in respiratory disorders, and have proven quite effective in mild chronic affections of the mucous membranes, including **bronchitis, pharyngitis, laryngitis,** etc.

It is a constituent of the official *mistura glycyrrhizæ composita* (U. S. P.), of mistura ammonii chloridi (N. F.).

The value of ammonium chloride troches, or lozenges, for local stimulation in **pharyngeal disorders** is well known. They serve the double purpose of increasing local lubrication by exciting the glandular acini and of gently stimulating the hepatic functions after the salt has been absorbed. The official ammonium chloride lozenge has already been referred to; 1 to 6 or more of these lozenges may be taken daily.

Ammonium chloride solution has also been used in throat affections in the form of a spray.

In Aural Disorders.—The use of chloride of ammonium vapor in affections of the middle ear has been prompted by its effectiveness in catarrhal affections of the nasal mucous membrane.

In Gastric Catarrh.—That ammonium chloride is of value in catarrhal disorders of the stomach, especially in children, is indicated by the frequency with which it is still resorted to. Presumably, its chief action is to loosen the mucous secretions. It may be given in solution or in pills; if in the latter form a half-tumblerful of pure water should be taken simultaneously to prevent undue irritation of the gastric mucosa by the salt. Instead of water, milk may be used.

In Cystitis.—In catarrhal cystitis ammonium chloride sometimes proves very effective. Ten grains (0.6 gram) every four hours on the first day, in a tumblerful of water, and 5 grains (0.3 gram) on the second day and thereafter soon cause the local distress greatly to diminish.

As a Stimulant to the Liver.—In all conditions associated with **torpidity of the liver**, whether this be due to a subacute hepatitis or to general asthenia, ammonia chloride, in doses of 20 grains (1.3 grams) three times a day, has been found of great value.

In Alcoholism.—In alcoholic intoxication ammonium chloride has been said to act as effectively as ammonia. Thirty grains (2.0 grams), repeated in half an hour, were found to bring the sufferer to his normal condition, in so far as the mental aberration was concerned. If emesis or lavage had been resorted to before the administration of the salt, the action of the latter was greatly prolonged.

In Neuralgia and Migraine.—Ammonium has been found frequently to afford considerable relief in these disorders, especially if given with tincture of aconite. Twenty grains (1.3 grams) of the ammonium salt with 2 minims (0.12 c.c.) of the tincture, repeated twice after the first dose, at intervals of half an hour, usually procured marked diminution of the suffering.

External Uses.—In superficial inflammatory swellings, *e.g.*, **buboes, mammary abscesses, testicular inflammations,** etc., ammonium chloride solutions have been applied locally with benefit.

In **vaginitis** a solution of 3 drams (12.0 grams) of ammonium chloride in 1 pint (475 c.c.) of water can be used as an injection or applied on a tampon with benefit (Butler).

A saturated solution of the salt may be used with advantage in **bruises,** to reduce swelling and diminish discoloration. The antiseptic qualities of ammonium chloride in the treatment of **wounds** have been emphasized by H. C. Wyman, who obtained good results, especially in contused wounds, from the use of gauze steeped in a solution of 1 ounce of the salt in half a pint of water. The circulation of blood in the injured parts also appeared to be improved by it.

In **senile gangrene** a good therapeutic measure is to place the foot in a solution of 8 ounces (250 grams) of ammonium chloride to 1 gallon (3800 c.c.) of water (Butler). It increases the alkalinity of the blood and thereby its osmotic properties, and facilitates its circulation.

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AMMONIUM ICHTHYOL GROUP. See Ichthyol.

AMPUTATIONS and RESECTIONS. See Resections, Amputations, etc.

AMYL NITRITE. See Nitrites.

AMYLENE CHLORAL. See Dormiol.

AMYLENE HYDRATE. — This substance is chemically tertiary amyl alcohol or dimethylethylcarbinol [$(CH_3)_2C(C_2H_5)OH$]. It occurs as a colorless, volatile, oily liquid, having an unpleasant ethereal odor and a burning, camphor-like taste. It is produced by the interaction of amylene, water, and sulphuric acid. Its specific gravity at ordinary temperatures is 0.820, and its boiling point is 99°-103° C. It is soluble in 8 parts of water and mixes freely with alcohol, ether, chloroform, and glycerin. It should be kept in well-stoppered bottles.

DOSE AND MODES OF ADMINISTRATION.—The dose of amylene hydrate taken by the mouth, for adults, is 30 to 90 minims (2 to 6 c.c.). If it is to be administered by the rectum, slightly larger amounts are required.

The disagreeable taste of amylene hydrate may be avoided by enclosing it in capsules (15 minims in each; 3 capsules at a dose) or by administering it in flavored solutions such as the following:—

℞ *Amylene hydrate*. 1 dr. (4 Gm.).
Water ..... 2 oz. (60 c.c.).
Orange-flower water ..... 2 oz. (60 c.c.).
Syrup of bitter orange ..... 1 oz. (30 c.c.).
M.

Of this one-half may be taken at night.

Where an analgesic effect is required in addition to the hypnotic influence, morphine may be combined with amylene hydrate, as in the following formula, recommended by Fisher:—

℞ *Amylene hydrate*. 1½ drs. (6 Gm.).
Morphine hydrochloride ..... ¼ gr. (0.015 Gm.).
Distilled water .. 3 oz. (90 c.c.).
Extract of licorice ..... 2½ drs. (10 Gm.).
M. Sig.: To be taken in two doses two hours apart.

Amylene hydrate may also be given in wine, beer, or brandy. A mixture of wine and syrup of licorice forms an especially good vehicle.

It cannot be employed subcutaneously, owing to the severe irritation and pain produced.

PHYSIOLOGICAL ACTION.—Amylene hydrate, like alcohol, causes a primary apparent excitement followed by depres-

sion and ultimate paralysis of the nerve-centers. The brain, cord, and medulla are stimulated and depressed in succession, the secondary results being sleep, abolition of reflex activity, and respiratory arrest. In the lower animals large doses have been found to induce cardiac depression and a pronounced fall in the body temperature. The latter effect has been credited to a direct action of the thermic centers. In man, however, amylene hydrate in moderate doses does not influence the temperature to any degree, even in fever. Neither does it depress to any marked extent, except in grossly excessive doses, the cardiovascular functions and respiration,—a feature in which it is superior to chloral hydrate. Amylene hydrate has but little influence on general metabolism. The elimination of urea is said to be more or less diminished after its internal use.

Locally, it is somewhat of an irritant. Upon subcutaneous injection tissue necrosis and abscess formation may result.

UNTOWARD EFFECTS; POISONING.—According to Scharschmidt, some patients perspire freely at the beginning of the effects of amylene hydrate. Occasionally excitement similar to that produced by alcohol or slight degree of stupor are produced by it. Headache and dizziness in a few instances follow its use.

Four cases of poisoning from overdoses were witnessed by Dietz. The symptoms consisted of deep sleep, from which the patients could not be aroused, complete motor paralysis, and loss of sensibility, including both touch and pain. The pupils were dilated, and reacted but slowly to light; the corneal reflex was abolished. Respiration was slow, superficial, and irregular; the pulse small, soft, and infrequent, and the temperature, in two instances, lowered to 95° F. Artificial respiration was required in one case. During recovery mental confusion and motor inco-ordination were conspicuous. In each case the overdose had been taken through neglect to shake the bottle in which the drug was mixed with syrup. Dietz advises that to avoid such accidents the drug be administered in capsules.

No instances of amylene-hydrate habit or cachexia have been observed (Flint).

THERAPEUTIC USES.—Amylene hydrate was introduced in medicine as a hypnotic by von Mehring, and has since held a favorable position as such, though, as Cushny states, it "has not received so wide a trial as it would seem to merit." Its effects rather closely resemble those of paraldehyde, but it leaves no bad taste in the mouth or disagreeable odor on the breath, such as are noticed with paraldehyde after the patient has awakened. In hypnotic power it is stronger than paraldehyde, but weaker than chloral hydrate. Likewise it is believed to exert a greater depressing influence on the heart than paraldehyde,—though less than chloral hydrate. Kirby and Griffith recommended that this drug be always used in heart disease in place of chloral. They also stated that in their experience amylene hydrate did not lose its efficiency upon continued use,—though given during three months in some cases,—and that the deep and refreshing sleep produced by the drug was praised by patients oftener than in the case of any other hypnotic.

Amylene hydrate differs in its action from chloral in that it does not increase nitrogenous wastes. According to Peiser the quantity of nitrogen eliminated by the urine after amylene hydrate is, in fact, lessened. This author therefore prefers the drug to chloral whenever the hypnotic effects are to be continued for a long time and in all affections associated with an exaggerated decomposition of albumins,—in fever, in anemia, pulmonary tuberculosis, and diabetes.

Sleep follows the ingestion of amylene hydrate much more promptly than after sulphonal, and it does not tend, as does the latter, to produce drowsiness and giddiness on the following day.

On the whole, amylene hydrate is, according to Kirby and Griffith, a reliable hypnotic if given in sufficient dose, though it is somewhat less certain in effect than chloral or morphine. When given by the rectum (in an enema with gum arabic and water), amylene hydrate brings on sleep in fifteen to forty-five minutes, or even sooner, though occasionally it fails entirely to do so.

Amylene hydrate acts satisfactorily in insomnia associated with nervousness, ex-

cessive **mental strain, fevers,** and **anemia.** Its usefulness in **cardiac states** has already been referred to.

In **gastric disorders** its oral use is apt to result in local irritation and nausea; in such cases it should be administered by the rectum. It is less irritating to the rectal mucous membrane than chloral hydrate.

In the insomnia of **mental diseases,** amylene hydrate has seen extensive service. In a series of 149 cases Lehmann obtained good results with it. In **mania** large doses were required. Cases of **paralysis of the insane** were benefited, but in the insomnia of **melancholia** it was less effective. It proved to be more efficacious and less unpleasant than paraldehyde.

Avellis found amylene hydrate generally effective in **alcoholic delirium.**

In a case of **opium addiction** in which chloral, bromides, paraldehyde and hyoscine, singly or variously combined, had given indifferent results, amylene hydrate produced sleep lasting through the night with but little or no intermission (Kirby and Griffith). Like results have been noted by other observers.

In **pulmonary disorders,** G. Mayer found amylene hydrate not only to produce sleep, but apparently to exert a decided sedative influence on the cough. In **tuberculosis** it sometimes proved useful in this respect after morphia had had but little effect. When there was pain or very troublesome cough, however, it was not uniformly successful. S.

AMYLOFORM.—Amyloform is a condensation product of formaldehyde and starch, first prepared by Classen, of Aachen, in 1896. It occurs in the form of very fine, white, odorless, and tasteless powder, which is insoluble in ordinary solvents. It remains undecomposed at a temperature of 180° C.

PHYSIOLOGICAL ACTION.—Amyloform is but slightly irritating. It is strongly antiseptic, disinfectant, deodorant, and absorbent, and is said to have all the advantages of iodoform without possessing its disagreeable odor. When applied to living tissue it is broken up into its two components,—formaldehyde and starch,—as shown by the fact that formaldehyde can be detected in the purulent discharge from suppurating wounds to which it has been applied (Classen). No symptoms of general intoxication are produced by the application of amyloform, though temporary smarting sensation locally is sometimes complained of. The secretions from open surfaces are rapidly checked by it.

THERAPEUTIC USES.—The drug is employed either as a dusting powder or in an ointment. Its uses are much the same as those of iodoform. Bongartz employed it with success in cases of **deep wounds** with **bone suppuration** and in **varicose ulcers** of the leg. Heddaeus laid stress on its rapid disinfecting action on **tuberculous lesions.** Its most important use, according to this author, is in the treatment of **superficial suppurative affections.** Lougard and Beauchamp used the drug in numerous cases of **phlegmon, abscess, furuncle,** etc., including **gynecologic affections.** Krabbel, who tested it both bacteriologically and clinically, came to the conclusion that amyloform was in no way inferior to iodoform as an antiseptic. C. L. Schleich, however, contends that it holds free starch, which smears up the wound and greatly hinders favorable action of the formaldehyde it contains.

Contrary to iodoform, amyloform can be sterilized in dry or moist heat without being decomposed. Because of this property, amyloform gauze affords some assurances of asepsis which are not found in the other antiseptic gauzes. An emulsion for preparing amyloform gauze is:—

℞ *Amyloform*.75 grs. to 2½ drs. (5-10 Gm.).
Glycerin ... 2½ drs. (10 Gm.).
Alcohol ....12½ drs. (50 Gm.).
Ether .....10 drs. (40 Gm.).
Ol. ricini .. 7½ mins. (0.5 Gm.).

The indications for amyloform are the same as for iodoform. (Presse méd., Sept. 15, 1900.)

Good results obtained with amyloform. The writers prefer it to the latter drugs in incised **abscesses, ulcers, wounds, burns,** and **purulent otorrhea.** Besides being harmless and free from any compromising odor, it remarkably hastens cicatrization. Cipriani (Monats. f. prakt. Dermat., Oct. 15, 1900).

Amyloform used in fresh and neglected **wounds, ulcers of the leg, excoriations, intertrigo, felons, carbuncles, osteomyelitis, tuberculous ulcerations,** etc. The pure powder usually employed. This occasions slight burning in sensitive patients, which, however, disappears soon. The chief features of its action are that it hastens granulation, diminishes secretion, and is, as a rule, non-irritating. Its freedom from odor and toxic effect is also noteworthy. A. Gerlach (Therap. Monats., Bd. xvi, Nu. 10, 1902). S.

AMYL VALERATE (Amyl Valerianate).—This is the isoamyl ester of isovaleric acid, and is a reaction product of amyl alcohol with sulphur and valeric acids. It represents the odoriferous principle of the apple, and occurs as a colorless liquid of specific gravity 0.858 and boiling point 190° C. (374° F.). It is insoluble in water, but dissolves in alcohol, ether, and chloroform. When in dilute solution, its ethereal apple-like odor is plainly evident.

PHYSIOLOGICAL ACTION.—Cider has long been believed by the laity to exert some favorable effect on calculous formations, and this seems to be borne out by the fact that amyl valerate actually does possess a certain solvent power with reference to cholesterin. Fifteen grains of cholesterin are dissolved by 70 grains of amyl valerate at 99° F., and by 46 grains at 104° F. Where the amount of cholesterin present exceeds the dissolving power of the valerate, it is, nevertheless, greatly softened,—to the consistency of gelatin.

The ingestion of amyl valerate induces primary general excitation and acceleration of the pulse, followed by somnolence (Pouchet). In addition to modifying or dissolving cholesterin, it tends to relax the bile-duct when in spasm.

THERAPEUTIC USES.—Amyl valerate was introduced by Blanc as an antispasmodic for use in **hepatic** and **renal colic,** and as a solvent for cholesterin calculi. It is said in hepatic colic not only to overcome the acute attack, but to prevent recurrences. No solvent effect on renal calculi is, however, claimed for it. The drug is administered in capsules; a capsule containing 2 to 6 minims (0.12 to 0.4 c.c.) may be given every half-hour, or one containing a somewhat larger amount, three times daily. The use of amyl valerate should be continued for some days after the acute disturbance has subsided.

Amyl valerate has also been employed in **muscular rheumatism,** in **dysmenorrhea,** and as a sedative in **hysteria.** S.

ANALGEN (quinalgen; labordin) is, chemically, the benzoylamido derivative of orthoethoxyquinoline [$C_9H_5.(OC_2H_5)$-$N.H.(CO.C_6H_5)N$]. It bears the same relation to quinoline as acetphenetidin does to benzene, with the exception that in analgen the benzoyl group takes the place of the acetyl in acetphenetidin. With the exception of thallin and thermifugin, it is the only member of the quinoline group of coal-tar analgesics or antipyretics which is still occasionally prescribed. It occurs in the form of colorless, tasteless crystals, soluble in hot alcohol and in acidulated water, slightly so in cold alcohol, and insoluble in pure water.

PHYSIOLOGICAL ACTION.—Analgen possesses the same antipyretic and analgesic properties as acetphenetidin, and its mode of action is closely similar (*v.* Acetphenetidin). With large doses, the same circulatory depressant tendency is present as with other coal-tar drugs. Analgen is more toxic than acetphenetidin, though less so than acetanilide. It is the least dangerous of the quinoline derivatives.

Analgen given experimentally to mammals induces motor depression and diminished reflex response, followed, with toxic doses, by cyanosis and convulsive movements.

The effects of analgen, when it is ingested, begin only after the benzoyl group in it has been set free by the gastric juice. Its action is, therefore, somewhat slower in appearing than is the case with acetanilide and antipyrin, and is to a certain extent inconstant.

A special feature of the action of analgen is that in large doses or upon continued use it produces a reddish discoloration of the urine. This coloration, when slight, is rendered more marked by the

addition of acetic acid (1 to 10). According to some, the coloration is due merely to the presence of decomposition products of analgen in the urine; according to Moncorvo, on the other hand, it is due to blood-coloring matter.

THERAPEUTIC USES.—The average dose of analgen for adults is 7½ grains (0.5 Gm.). According to Goliner, the maximum single dose is 15½ grains (1.0 Gm.) and the maximum daily amount 45 grains (3 Gm.). The drug has been used chiefly as an antineuralgic and antipyretic. Of late its use has, however, greatly diminished, the official drugs acetanilide, antipyrin, and acetphenetidin meeting with greater favor. Besides, the use of any antipyretic has justly lost favor.

Scholkow, Foy, Spiegelberg, and Maas found analgen effective in a large number of cases of **neuralgia.** According to Foy, who used it in 200 patients, the full dose of 15 grains (1.0 Gm.) was necessary to produce relief. In the pains of **tabes, zona,** and **hysteria,** the results were less brilliant, but in **acute articular rheumatism** and **muscular rheumatism** distinct benefit was noted in many instances. According to Maas, patients suffering from **pulmonary tuberculosis** experience "a peculiar feeling of well-being" from its use. Moncorvo used analgen in 59 children, 33 of them presenting various **malarial** manifestations, with satisfactory results. It was readily taken, because tasteless, and in no instance exerted any unfavorable action of the circulation or respiration. The urine became colored a deep yellow or red, but albumin and sugar were never detected. It acted satisfactorily as a sedative in **chorea,** hysteria, and **partial epilepsy** and was found useful to relieve **pain** of various kinds, including that of **Pott's disease** and **hip-joint tuberculosis.**

Occasional instances of untoward secondary effects are recorded by Scholkow and Spiegelberg, including headache, tinnitus, nausea, diarrhea, and tremor. Patients taking analgen should be informed of the red discoloration likely to appear in the urine, lest they be unduly frightened thereby. S.

ANEMIA. See ANEMIA, SECONDARY.

ANEMIA, PERNICIOUS PROGRESSIVE. — DEFINITION. — A form of secondary anemia characterized by a progressive destruction of the red corpuscles which tends toward a fatal issue.

SYMPTOMATOLOGY.—Pernicious anemia develops insidiously, though an abrupt onset occasionally occurs, especially in pregnant or puerperal women. The most evident symptom is pallor of the face and body, which gradually becomes extreme and assumes a lemon-yellow tint. This yellowish color deepens as the case progresses; it may appear suddenly, but in the majority of cases it develops gradually, following the insidious course of the disease. The mucous membranes are similarly affected.

There is great weakness with all its attending symptoms: inordinate palpitations and dyspnea on exertion, sighing, and slow delivery in speaking. The pulse, which may be strong at first, is regular, but rapid, soft, and compressible, in the majority of cases, more or less fever being usually present. The temperature is extremely irregular. Slight evening pyrexia is seldom absent in advanced cases.

Cardiac murmurs, especially of the hemic type, are usually to be heard, especially at the base, and signs of fatty degeneration may be detected by auscultation, although there is usually no arterial degeneration or valvular disease. A loud venous hum can sometimes be detected in the vessels of the neck, the so-called *bruit de diable* with exaggerated cardiac impulse. Edema of the ankles, face, and lungs and dropsical effusions may appear at any stage.

Retinal hemorrhage is a symptom of great value. The ophthalmoscope may thus reveal the cause of the so-called

"anemic amaurosis" observed in these cases, though the whites of the eyes are pearly and the conjunctivæ pale. There may also be hemorrhages into the mucous membranes, epistaxis, menorrhagia, and purpuric eruptions in advanced cases. Ecchymoses in the skin and mucous membranes are sometimes noticeable in advanced cases.

Retinal hemorrhages are also witnessed.

In the diagnosis of pernicious anemia examination of the retina is of great

Fundus oculi in a case of pernicious anemia, showing retinal hemorrhages. (*Bramwell.*)

value, especially in those cases in which the blood-picture is indefinite. In about 47 out of 50 cases of pernicious anemia, retinal hemorrhages were found to be present; while in 51 cases of severe secondary anemia, in which the hemoglobin was below 50 per cent., and in 121 cases with a hemoglobin of 50 per cent. to 70 per cent., retinal hemorrhages were never found. In 72 instances of malignant tumor (43 of carcinoma and 29 of gastric carcinoma) in which there is especially liable to be confusion with pernicious anemia, the writer never saw retinal hemorrhages. Not only does the presence of hemorrhages favor the pernicious type of anemia, and their continued absence a secondary anemia, but they are of prognostic importance as well. The retinal hemorrhages are larger and more numerous in the severe cases, and clearing up of the hemorrhages is one of the earliest indications of beginning improvement. Hesse (Deut. med. Woch., Aug. 12, 1909).

Gastric and intestinal disorders are the rule, although the general nutrition is apparently preserved, the appetite being sometimes voracious, and the patient becoming obese. Nausea is frequently an early symptom. Dyspepsia, vomiting, and diarrhea usually prevail, though some cases suffer from constipation. The gastric region is tender to pressure, and the tongue is pale and smooth. Eructations and anorexia are common. Involvement of the osseous system is occasionally indicated by sensitiveness of the bones, especially those of the sternum.

The respiration is usually accelerated, and dyspnea, air-hunger, and oppression in the chest are frequent symptoms. Pericardial and pleural effusions are sometimes observed.

Drowsiness is present in the majority of cases, but insomnia is occasionally noted. The patient is readily fatigued and even exhausted on the least exertion. The weakness increases until attacks of faintness supervene. The patient ultimately becomes bedridden.

Headache, vertigo, tinnitus, apoplectiform attacks, delirium, and other disorders of the nervous system, such as paresthesia, neuralgia, and extensive paralyses, have been noted. Mental torpor, somnolence, peevishness, confusion, delirium, and various psychic phenomena may also occur.

Case in which there were not only symptoms of spinal cord disease, but a peculiar psychosis existing as well in connection with the pernicious anemia.

Changes in the psychic function have seldom been mentioned in relation with pernicious anemia. Disturbances as a result of a mere anemia, such as lowered mental capacity, occur, according to Strumpell. Consciousness is retained, but the mental processes are dull and apathetic. In most textbooks of psychiatry anemia is given as an important cause of various psychoses, especially of mental confusion and delirium. Mental disturbances, other than indolence, apathy, and somnolence, except delirium just before death, have not been mentioned. Henry Marcus (Neurol. Centralbl., May 16, 1903).

A number of patients have been observed whose chief symptoms were of a distinctly mental and nervous character, but who in the course of time were found to present the characteristic blood conditions and bodily signs of pernicious anemia. In some, the nervous and mental symptoms appeared to be secondary to, in others to precede the development of, the anemia. Clinically, these cases collectively have seemed to present a rather characteristic syndrome, the principal features of which are as follows: 1. General ill health. 2. Mental symptoms, viz., intermittent attacks of loss of inhibition, peevishness, and gradual mental deterioration. 3. Sensory disturbances: (*a*) Subjective, consisting of intramuscular and articular dull aches and pains, seldom accompanied by effusion and never by true inflammatory action. With these, and perhaps rather more frequent, are sensations of numbness, tingling, and weight in the extremities, especially the legs. (*b*) Objective sensory disturbances: These are common and consist in patchy losses of pain and tactile sensibility about the feet and ankles. Sometimes there may be only retardation of sensation at first. Tabes is excluded by the other positive and negative symptoms. 4. Plus knee jerks, ankle clonus, and the Babinski sign are sometimes present. 5. Ataxia of gait and station is often present. 6. Diarrhea of the mucous types is apt to occur sooner or later. 7. The peculiar lemon-yellow tint of pernicious anemia occurs in the later stages. A combination of all these signs or a majority of them should suggest the possibility of a pernicious or prepernicious anemia, and a careful blood examination may then confirm the diagnosis. Eight cases more or less typical of the condition are reported. F. W. Langdon (Jour. Amer. Med. Assoc., Nov. 25, 1905).

Absence of the knee-jerk is frequent, and is indicative of degeneration of the posterior columns of the cord.

Jaundice is occasionally met with. The urine is dark and highly colored; it is of low specific gravity, and shows an increase of urea and uric acid and pathological urobilin. Indican may also be detected.

When the end is approaching, the temperature, which in the course of the disease is apt to rise toward evening, sometimes reaching as high as 102° F. (38.8° C.), recedes markedly, and the patient enters into a torpid condition ending in coma.

BLOOD EXAMINATION. — Before describing all the characteristics of the blood, a summary of its morbid changes may prove useful. Though sometimes dark and watery, the blood is, as a rule, pale. The red corpuscles are greatly reduced, sometimes as low as 143,000, though, as a rule, they do not go below 500,000. The percentage of hemoglobin is also greatly reduced, but not in proportion with that of the red corpuscles. The latter also show considerable alteration in size and shape. Some are large and ovoid (megalocytes); others are small, round, and dark red (microcytes), while others again are very irregular in shape (poikilocytes). Nucleated red cells, both normoblasts (normal in size) and megaloblasts (when very large), are a marked characteristic of the disease, while blood-plaques are either absent

or present in very small number. The leucocytes, though relatively increased in respect to the red corpuscles, are usually normal in number, with the smaller mononuclear forms predominating.

To understand these blood changes, however, they must be analyzed from the standpoint of their cause. The two prevailing theories as to the pathogenesis of pernicious anemia are: 1. That the disease is due to breaking up of the blood-corpuscles (hemolysis). 2. That, owing to some defect in the blood-making (hemogenesis), the blood becomes vulnerable to the destructive influence of micro-organisms. At the present time the former view strongly prevails, the hemolysis, as urged by Grawitz, Hunter, Stengel, and others, being ascribed in great part to poisons absorbed from the alimentary canal, the disease being thus an autointoxication. The toxics, according to Sajous, promote and sustain hemolysis by causing an overproduction of antibodies, which not only destroy the pathogenic poisons, but also the red corpuscles.

> By the subcutaneous injection of the muriate of phenylhydrazin into animals a condition of the blood similar to that in pernicious anemia is obtained. S. Kaminer and R. Rohnstein (Berl. klin. Woch., July 30, 1900).
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> Pernicious anemia is probably due to an intoxication, possibly from the stomach, and the cases referred to are probably to be placed in the same category. It is easily understood that with an absence of free hydrochloric acid enormous bacterial growth can take place in the intestines, and that changes in the digestion of the proteids will follow. The treatment of the condition is self-explanatory. Grawitz (Berl. klin. Woch., June 29, 1903).
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> Pernicious anemia is a definite hemolytic disease with disturbances of the alimentary canal and fever. The course of the disease is marked not only by slight variations from time to time, but usually by one or more periods of distinct improvement, lasting sometimes many months, in some cases even a year or two—sometimes occurring independently of treatment, but without doubt greatly due to the beneficial effect of arsenic. The tendency to relapse is in reality due to the remarkable persistence of the specific hemolytic infection underlying the disease, since it is always accompanied by a recrudescence of the lesions in the tongue, stomach, or intestine, and by the glossitic, gastric, or intestinal symptoms connected therewith. Hunter (Brit. Med. Jour., Nov. 9, 1907).
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> In an attempt to isolate a hemolytic substance from the stools of patients suffering from pernicious anemia with ulceration of the intestines, the authors studied the stools from 106 cases, all but 11 of which showed some gastro-intestinal lesion. A hemolytic substance was constantly found in the stools of patients suffering with tuberculous enteritis (10 out of 11 cases), while normal cases gave practically negative results. The hemolytic substance appears in the stools whenever there is a disturbance of fat absorption. Grafe and Rohmer (Deut. Archiv f. klin. Med., Bd. xcvi, S. 397, 1909).

Deficiency of red corpuscles (oligocythemia) is always very great; the blood is, therefore, pale and thin, resembling sherry wine. The oligocythemia is sometimes so marked that the normal proportion of 5,000,000 red corpuscles to the cubic centimeter is reduced to one-twenty-fifth of that number. Quincke reported a case in which, as previously stated, there were only 143,000 to the cubic centimeter immediately before death. This is an important diagnostic feature. There is no disease, except pernicious anemia, in which the number of red corpuscles is at any time reduced below 20 per cent. This affords a distinction between

pernicious anemia and latent gastric cancer, a disease with which the former is most likely to be confounded.

The hemoglobin is also greatly reduced (oligochromemia), but not in proportion with the cell reduction. The hemoglobin percentage was greater by 10 per cent. in a case seen by Osler. The relatively high percentage of hemoglobin depends upon increased average size of the corpuscles and in some cases on the presence of an unusual number of highly colored and minute microcytes. It also depends, in a measure, upon the time at which the examination is made. The icteric color of the skin and the dark urine are caused by dissolution of the red blood-corpuscles, and the hemoglobin estimated at one of these periods will thus be higher, owing to the more highly colored plasma. The red blood-corpuscles show marked signs of reversion to the type of blood which is normal in the cold-blooded animals.

There is also a species of degeneration closely resembling coagulation necrosis, and an alteration of the corpuscles, characterized by the appearance in their interior of certain corpuscles composed of modified hemoglobin—*dégénération hémoglobinémique*.

The process of regeneration is manifested by the presence of nucleated red corpuscles, which are divided by Ehrlich into two varieties: the normoblasts and the megaloblasts, the former corresponding to the hematinic evolution of adults, the latter to that of the embryo. The nucleus of the normoblast is extruded to form a new red corpuscle, while the nucleus of the megaloblast is absorbed. Fresh blood shows nucleated red corpuscles of large size, the megalocytes and gigantocytes previously mentioned.

Fürbringer has shown that a case is to be considered as one of true pernicious anemia only when one-fourth of the red corpuscles are macrocytes. The presence of megaloblasts is a sign that certain pathological changes are taking place in the red marrow rather than a distinctive feature of pernicious anemia. The macrocytes are more characterisic of pernicious anemia, because they are the direct precursors of the large red-marrow cells.

Misshapen corpuscles (poikilocytes) are very frequently observed, oftener, indeed, than in any other affection. Many small, imperfectly developed corpuscles (microcytes) are generally found.

In marked cases corpuscles endowed with motion are occasionally observed. According to Hayem, the red blood-corpuscles of normal blood are motionless. Conversely, the elements observed in cases of high degree of anemia are endowed with four kinds of motion: 1. A movement of the entire mass of the corpuscle. 2. The projection of mobile prolongations. 3. A movement of oscillation, manifested slowly by minute corpuscles. 4. A movement which results in changing the position of the corpuscles. These movable corpuscles are bodies arrested in their evolution and still retaining the contractile properties of the hematoblasts from which the red corpuscles originate. On superficial examination they might readily be mistaken for parasites.

Many years ago I observed distinct movements in the red corpuscles in a case of pernicious anemia, but made no public mention of the interesting fact. Senator has also called attention to the presence of small, mobile bodies observed staining the same as red corpuscles and resembling fragments of

hematin, thought to possess pathognomonic value.

Pernicious anemia is essentially a hemolytic disease, the hemolysis being due to some as yet unknown poison comparable in its effect on the blood and blood-organs to the action of toluylenediamine—whether autointoxication or infection remains yet to be determined. The poison of pernicious anemia stimulates the phagocytes of the spleen, lymph- and hemolymph-glands, and bone-marrow to increased hemolysis (cellular hemolysis). Either the phagocytes are directly stimulated to increased destruction of red cells or the latter are so changed by the poison that they themselves stimulate the phagocytes. The hemolysis of pernicious anemia differs only in degree, not in kind, from normal hemolysis or the pathological increase occurring in sepsis, typhoid, etc. It is not improbable that from the destruction of hemoglobin poisonous products (histon?) may be formed which have also a hemolytic action; a vicious circle of hemolysis may thus be produced. No proof of this exists at present. The hemolysis of pernicious anemia is not confined to the portal area, as according to Hunter, but, in some cases at least, takes place also to a large extent in the prevertebral lymph- and hemolymph- nodes and bone-marrow. In the majority of cases the spleen is the chief seat of the blood destruction. No evidences of hemolysis in the liver, stomach, and intestinal capillaries were found in the 8 cases. The hemosiderin of the liver and kidneys is carried to these organs as some soluble derivative of hemoglobin, is removed from the circulation as hemosiderin by the endothelium, and then transferred to the liver- or kidney- cells. The deposit of iron in these organs is of the nature of an excretion. In the majority of cases only slight reaction for iron is found at the sites of actual hemolysis (spleen, lymph- and hemolymph- glands, and bone-marrow). The greater part of the pigment in the phagocytes of the spleen, lymph- and hemolymph- glands does not give an iron reaction while in a diffuse form. When changed to a granular pigment the iron reaction may usually be obtained. The change to hemosiderin is for the greater part accomplished by the endothelium of the liver and kidneys. The varying pathological conditions found in these different cases of pernicious anemia can be explained only by a theory of cyclical or intermittent process of hemolysis. This theory is also borne out by the exacerbations so frequently seen clinically. The autopsy findings, in so far as evidences of hemolysis are concerned, will depend on the relation between the time of death and the stage of the hemolysis. The changes in the hemolymph-glands found constantly in these 8 cases were: dilatation of the blood-sinuses and evidences of increased hemolysis, as shown by the increased number of phagocytes containing disintegrating red cells and blood-pigment. In some of the cases these changes were accompanied by great increase in size and apparent increase in the number of hemolymph-glands; in other cases there was no hyperplasia, the only evidence of the changes present being that obtained by the microscopic examination. The changes found cannot be regarded as a specific of pernicious anemia, since it is probable that they may be produced by other infections or toxic processes characterized by great hemolysis. The lymphoid and megaloblastic changes in the bone-marrow do not form an essential part of the pathology of pernicious anemia, and are to be regarded as of a compensatory nature: an increased activity of red-cell formation to supply the deficiency caused by the excessive hemolysis. A. S. Warthin (Amer. Jour. Med. Sciences, Oct., 1902).

PATHOLOGY.—In cases in which the urine is dark the latter is found to contain pathological urobilin: a substance known to be derived from the disintegration of hemoglobin, and which, according to Hunter, is of high diagnostic significance. A peculiarity

of this highly colored urine is that it presents a low specific gravity, averaging 1.014. Occasionally, however, the urine is habitually pale. The kidneys are often the seat of fatty infiltration, accompanied sometimes by thickening of the interstitial tissue.

Case in which hemolysis in pernicious anemia was augmented by urinary retention. The urinary retention was secondary to relapses of the anemia which caused weakness of the bladder musculature. Cunningham (Annals of Surg., Feb., 1907).

Case similar to Cunningham's, but in which an enlarged prostate, which was present in both cases, was primarily responsible for the urinary retention. Following this there was a retention and absorption of the hemolysins which failed to be excreted, with consequent changes in the course of the disease. When the poison that is normally being excreted from the kidneys is added to that in the general circulation, increased hemolysis is to be expected. H. A. Freund (Jour. Amer. Med. Assoc., May 4, 1907).

Examination of the kidneys in 12 cases of pernicious anemia of unknown etiology showed that in every instance fat was present in the kidneys, but in slight amount and in special arrangement in the cells, being rather of the nature of a fatty infiltration than a degeneration of the renal epithelia. In long-continued or very rapidly progressing cases focal deposits of furruginous pigment were present, but only in the cortical substance in the epithelia of the convoluted tubules. In all cases there was a marked increase and thickening of the interstitial tissue resembling sclerosis, most pronounced in the medullary substance. L. Paszkiewicz (Virchow's Archiv f. Path. Anat., Bd. cxcii, S. 324, 1908).

Case illustrates the relations between pernicious anemia and renal lesions. A man aged 52 years came under treatment for a grave anemia, weakness, and generalized edema. The patient grew steadily worse, and died in apparently uremic coma. The examination of the blood showed an intense plastic anemia with myeloid reaction and hyperleucocytosis; some nucleated reds were present, and the corpuscular resistance was normal. At autopsy the main lesion present was nephritis with a kidney of the large white type. The factors of dilution of the blood, toxic hemolysis, or a defect in the corpuscular resistance the authors do not think can enter into this case. It is possible, however, that both the renal and blood lesions are the result of some infection or intoxication. At any rate, this association of the two lesions is frequent and should be noted in a condition the cause of which is so often unknown. Labbé and Joltrain (Arch. des mal. du cœur, des vaisseaux, et du sang, vol. i, p. 366, 1908).

The gastric and intestinal disorders are probably due to the formation of poisons, which, we have seen, act, in turn, as the etiological factors of the general disease. The gastric and intestinal walls are often found to be the seat of fatty change, and atrophied. Carious teeth have been regarded as potent factors in the etiology of pernicious anemia by Hunter, but this view has not been sustained. Intestinal entozoa, however, undoubtedly underlie many cases.

The writer considers that the causative process of infection is double: (1) a specific infection of which the chief evidence is a glossitis, and (2) a septic infection of the mouth, stomach, and intestine of which the chief evidences during life are varying degrees of "oral sepsis" and "septic gastritis," the latter recognizable during life by the vomit and various symptoms of oral, gastric, and intestinal disturbance, and after death by the conditions of gastritis, gastric and intestinal atrophy, and now and again erosions and ulcers. Sepsis alone is incapable of giving rise to true pernicious anemia, for in septic anemia there is no evidence in the liver of hemolysis. A peculiar form of

glossitis had been found in every one of the 25 cases included in the present paper. There was great thinning of the mucosa, which in places was entirely lost, so that the lymphatics of the tongue were left in direct continuity with the buccal cavity. This thinning of the mucosa produces the peculiar glossy surface of the tongue characteristic of the disease. Hunter (Practitioner, July, 1902).

Repeated intravenous injections of living cultures of the colon bacillus into rabbits found to cause the development of a state of advanced anemia not quite comparable with any of the classical forms seen in man. In some respects it resembles pernicious anemia, namely: in the very great diminution of erythrocytes, the marked poikilocytosis, and the appearance of nucleated red corpuscles. On the other hand, it differs from pernicious anemia in the fall of the amount of hemoglobin being parallel with the decrease of the red corpuscles, in the absence of a distinct and extensive Inincke's siderosis, in the absence of any clear evidence of inflammatory or other disturbances of the digestive tract, and of well-marked changes in the bone-marrow. In the advanced stage of this anemia a diffuse degeneration of the spinal cord was set up, affecting the posterior and lateral columns of the cord, in the lumbar and dorsal regions. This degeneration consisted in a fatty degeneration of the myelin sheaths of the fibers and certain pigmentary changes in the nerve-cell bodies of the gray matter. The ventral columns of the cord and the gray matter were not affected. Similar conditions of anemia and spinal-cord degeneration could not be produced by injecting killed cultures of the colon bacillus, nor by filtered cultures. When the living cultures were acted upon by pepsin, and injected intravenously, they did not differ materially in their action from the original living cultures. G. A. Charlton (Jour. of Med. Research, May, 1904).

Pernicious anemia may be due to an infection of the intestinal tract with the *Bacillus aërogcnes capsulatus.* The writer finds this organism regularly and in large numbers in the fecal matter of patients with pernicious anemia, whereas in ideal conditions of human digestion the organism is present only in small numbers. Reductions in the number of capsulati, in these patients, are followed by an improvement of symptoms. Neutral filtrates from cultures of this bacillus in blood bouillon were found to have a marked hemolytic power. Seventeen cases of anemia were studied, 9 undoubtedly pernicious, 4 probably pernicious, and 4 possibly belonging to the same class. Herter (Jour. of Biol. Chemistry, Aug., 1906).

The writer has found no oral sepsis in any of his cases, and does not believe this has the influence in the production of the disease which some authorities have suggested. The glossitis from which many patients who are affected with pernicious anemia suffer is a consequence rather than a cause, due, presumably, to the same toxin, whatever it may be, which is the cause of the anemia. Byrom Bramwell (Brit. Med. Jour., Jan. 22, 1909).

Tallquist has shown that *Dibothriocephalus latus,* which may cause an anemia similar to pernicious anemia, contains a powerfully hemolytic lipoid which can be extracted from the body of the worm, and has been able to demonstrate quite similar substances in the mucosa of the human digestive tract. The writers have pursued investigations of like nature, the results of which follow: 1. In pernicious anemia there is present in the gastric and intestinal mucosæ a lipoid substance soluble in ether, which is about ten times as powerful a hemolysin as the lipoid obtained from the normal mucosa 2. Tested experimentally on animals, this lipoid shows weak, but definite hemolytic properties when administered either subcutaneously or by the stomach. That obtained from the normal mucosa exerts much less action or none at all. 3. The resulting anemia has the characteristics of pernicious anemia. 4. In dogs it is possible to obtain a lipoid similar in action to that in pernicious anemia, after first producing

a gastrointestinal catarrh. 5. The conclusion seems justified that the origin of the so-called cryptogenic form of pernicious anemia is to be found in the hemolytic action of this lipoid material, with secondary insufficiency of the bone-marrow. 6. The place of origin of this powerfully hemolytic lipoid is in all probability the gastrointestinal mucosa; the cause of its production seems to be a chronic inflammation of the mucosa. Berger and Tsuchiga (Deut. Archiv f. klin. Med., xcvi, S. 252, 1909; Amer. Jour. Med. Sci., Sept., 1909).

Experimental research with the extract of the gastrointestinal mucosa after death from pernicious anemia and with the mucosa from dogs with gastrointestinal affections. The extract of the mucosa under certain conditions had a pronounced hemolytic action. It seems probable that an inflammatory infiltration in the gastrointestinal mucosa plays an important part in the development of pernicious anemia. The inflammatory catarrhal process leads to the production of an intensely hemolytic lipoid substance. That every catarrhal affection is not accompanied by anemia is due to the compensating action of the bone-marrow which replaces the destroyed blood-corpuscles as fast as they are destroyed. The process has to be very severe or very long continued to result in a pernicious anemia. Schmidt (Deut. Archiv f. klin. Med., Bd. xcvi, Nu. 3-4, 1909).

The spleen is generally thought to present no characteristic lesion, although the amount of iron in it is usually increased. It may, however, be slightly enlarged, and be the seat, as observed by Stanley, of sclerotic changes, along with similar changes in the pancreas and adrenals.

In every spleen finely granular cells, as myelocytes, found. Eosinophilic myelocytes and normoblasts are only seen in spleens which have suffered alteration through congestion, infectious processes, and severe anemias. Under certain conditions the spleen may undergo myeloid transformation, partly through the proliferation of the pre-existing myelocytes and partly through emigration to other cells, to which class belong the eosinophiles and normoblasts. Kurpjuweit (Deutsch. Archiv f. klin. Med., Bd. lxxx, p. 168, 1904).

Changes in the spleen and liver similar to those described by Meyer and Heinecke in man in pernicious anemia and in other severe anemias may be produced in animals by the administration of hemolytic substances; the writer's results confirm those obtained by Morris. In some instances, especially in chronic anemias with regeneration, the liver and spleen both resembled the organs of the embryo at the stage when these organs are engaged in hematopoiesis. Domarns (Archiv f. exper. Path. u. Pharm., Bd. lviii, S. 319, 1908).

Jaundice is probably due to accumulation of iron in the hepatic system. In a case studied by Ruttan and Adami, the total quantity of iron found in the liver was 0.2433 per cent. by weight calculated to the fresh undried tissue. This is equivalent to about 0.72 per cent. to the dried tissue. The estimation accords fully with the observations of previous observers, as showing the very great increase in the iron contained in the liver in this disease. Kelynack and Coutts found it to be five times greater than normal. The iron is mainly deposited about the periphery and middle zone of the lobules, and is derived from the vast number of destroyed red corpuscles. The kidneys, spleen, pancreas, hemolymph-glands are also laden with iron-pigment derived from these cells.

Inquiry into the after-history of 22 cases. The disease believed to be due to an increase in the destructive action of the liver upon the red blood-corpuscles. While the 22 cases were thought to be "cured" by various means, 10 died of the disease, and only 2 were known

to be living at the time of the investigation. H. C. Colman (Edinburgh Med. Jour., March and April, 1901).

Case of jaundice associated with weakness in which there were no abdominal symptoms or evidence of obstructive lesion of the bile-ducts. The blood-picture was typical of Addison's anemia. There was marked improvement of health and disappearance of jaundice under arsenic and appropriate hygienic measures. Vanderhoof (Old Dominion Jour. of Med. and Surg., April, 1911).

The posterior and lateral spinal tracts present changes resembling those observed in tabes, but most marked in the posterior lateral columns, as observed by Nonne, and to a less degree in the lateral columns. All these changes are not typical of pernicious anemia, however, and may be met with in other diseases in which cachexia and marasmus predominate, such as Addison's disease and diabetes. Hemorrhagic areas in the cord and brain due to hyaline degeneration of the blood-vessels are also met with. We have seen that retinal hemorrhages constitute a diagnostic feature of the disease.

Study of pathological lesions found in the spinal cord in cases of pernicious anemia showed that there was usually a degeneration affecting the posterior columns, sometimes the posterior and lateral together, but never the lateral alone. This degeneration was chiefly in the nerve-fibers, and was unaccompanied by shrinking of the cord, such as was seen in locomotor ataxia. Seventeen cases analyzed in which initial nervous symptom was always a persistent paresthesia, usually of the foot, associated with some weakness. This was generally followed quickly by ataxia and loss of motor power, and severe pains in the back and limbs were not uncommon. The disease progressed rather rapidly, so that often within one or two months the symptoms were well developed. In from six months to a year the progress commonly reached its acme, and during this time the anemia became marked. After a time the control of the bladder and the rectum was lost, and in fatal cases death occurred in from six months to two years. The essential nature of the process was a primary nerve degeneration affecting the neuraxons first, particularly in the columns of Goll and the crossed pyramidal tract. The same poison which caused pernicious anemia was responsible for this disease. It usually developed between the ages of 50 and 60 years, and followed the acute infections, prolonged diarrheal or dysenteric attacks, lead poisoning, malarial infection, etc. In 10 per cent. or more of the cases pernicious anemia undoubtedly coexisted. Charles L. Dana (N. Y. Med. Jour., Nov. 19, 1898).

Examination of the spinal cord in cases of pernicious anemia by the Marchi method. Results summarized as follows: (1) the changes in the spinal cord in fatal cases of anemia are not systematic, but should be regarded as acute disseminated myelitis; (2) the foci exhibit a local association with the blood-vessels; (3) it is probable that a noxious material is carried to the cord by the blood-vessels, and this acts upon the nervous tissue; similar changes are found in old age; (4) even in advanced cases the gray matter may escape involvement; (5) if diseased, it is not primarily affected,—that is to say, it and the white matter are involved as the result of a single cause; (6) the diffuse character of the degeneration in these conditions justifies the conclusion that there is a trophic alteration, and not a functional injury of the nervous element; (7) the greater part of degenerated fibers are found in the posterior roots and the anterior commissure. Nonne (Deut. Zeit. f. Nervenheilk., March 9, 1899).

There is a well-established relation of diffuse cord degeneration with pernicious anemia. It seems highly probable that the hemolysis and the cord changes are due to the same toxin. While the source of the toxin is unknown, the fact that gastrointestinal

disturbance is so common in the disease would lead one to suppose that it is of intestinal origin. The diffuse degenerations of the spinal cord which occur in conditions without pernicious anemia do not appear to differ essentially from those of pernicious anemia. It is possible that a common blood-circulating poison exists, which may expend its force upon the blood in one individual, upon the nervous apparatus in another, and coincidently upon the blood and spinal cord in others. Frank Billings (Boston Med. and Surg. Jour., Aug. 28 and Sept. 4, 1902).

Case which shows the alterations in the sympathetic nervous system in pernicious anemia. The celiac and superior cervical sympathetic ganglia were examined microscopically after having been stained by Nissl's method. The nerve-cells were found profoundly altered; in fact, in most of them the nucleus was either no longer visible or cloudy, deformed, and displaced toward the periphery of the cell. In many cells there was a granular pigment scattered through the protoplasm in the form of yellowish-brown refractile granules. In other places the protoplasm was found in a condition of fatty degeneration. In places the cell body was but very faintly visible, and the nerve-processes indistinct, atrophied, and in some cases fatty. G. Vincenzo (Gaz. degli osped. e delle clin., Sept. 23, 1900).

Out of 50 cases of pernicious anemia, about 20 showed nervous manifestations of one kind or another. The writer analyzed the cases with the view of classifying the nervous symptoms, but without determining any definite groups. At one end of the series are merely sensory disturbances, and at the other complete paraplegia with loss of control of bladder and rectum. Report of 3 cases as examples of different types. McCrae (Bull. Johns Hopkins Hosp., Feb.-March, 1902).

Two cases illustrating 2 of the types of nervous-system involvement. In the first case, which had the longest and more pronounced history of anemia, the nervous symptoms were at a minimum and the posterior columns of the cord, particularly in the cervical region, alone showed degeneration, characteristically patchy in distribution. In the second case, the nervous involvement, particularly in the later stages, overshadowed the anemia. Here the spinal cord presented very extensive, yet incomplete degeneration with slight replacement gliosis in the posterior columns, and also a similarly irregular, but more diffuse degeneration in the lateral tracts, which, however, was a rather less complete and apparently somewhat more recent process. Camac Milne (Amer. Jour. Med. Sci., Oct., 1910).

The bone-marrow usually presents changes which indicate abnormal activity, being composed mainly, when the case is not too far advanced, of hematoblasts, as emphasized by Rindfleisch. It resembles in this state, as noted by H. C. Wood, Pineau, and others, the hemoblastic marrow of childhood. Other changes frequently found, according to Muir, are (*a*) increased number of nucleated red corpuscles in the marrow; (*b*) transformation of the fatty marrow in the shafts of the long bones into red marrow; (*c*) absorption of the bone trabeculæ between the red marrow. Later, it presents all the signs of excessive compensative function, being actually hypertrophied in some instances. When this stage is reached the bone-marrow may lose its power to create red corpuscles.

The proteids of the plasma may be altered in their respective proportions, and considerably reduced—40 per cent. below the average normal quantity, according to Ruttan and Adami—the globulins being especially reduced.

As ill understood as the etiology of the disease is the actual condition of the blood. The microscopic appearances are well known, but the true chemical

changes have almost entirely been neglected. The blood in pernicious anemia contains a larger quantity of water than normal blood, a smaller quantity of solids, a higher proportion of chlorine, and a lower proportion of potassium, iron, and fat. There is not sufficient sodium to hold the chlorine fixed, and the potassium is also deficient. In various tissues the proportion of water was higher than normal in the heart, and lower in the liver, spleen, and brain. Treatment of pernicious anemia with potassium carbonate, tartrate, and citrate in 4 cases, 3 of which were dying, resulted in recovery. Th. Rumpf (Berl. klin. Woch., May 6, 1901).

Although fatty degeneration is present in practically all organs, emaciation is exceptional, though the adipose tissue is pale and yellowish, contrasting with the usually red muscular tissue. The heart, however, is enlarged and flabby, and its muscular elements are pale, friable, and fatty, its cavities containing light-colored blood. The general fatty degeneration affecting markedly the vessel walls, these are extremely friable; hence, the hemorrhages, retinal, cutaneous, etc., and the ecchymoses so frequently witnessed.

DIAGNOSIS.—While pernicious anemia possesses characteristics that readily distinguish it from other blood affections,—the color of the skin, the retinal hemorrhages, etc.,—the early stages are generally such as to suggest diseases that do not present the same degree of danger.

Benign Anemia.—Intractability of the disease, after the removal of supposed causes and the faithful use of appropriate measures of treatment, strongly suggests the presence of pernicious anemia.

Chlorosis.—From this affection pernicious anemia may readily be differentiated by the blood examination. Instead of relative increase of hemoglobin, the presence of gigantoblasts, marked oligocythemia, and macrocytes differentiate. The red corpuscles, in chlorosis, may be normal in number and size, the only change being a deficiency of hemoglobin. Again, the corpuscles may be normal in number, but diminished in size, while the percentage of hemoglobin is normal; finally, the corpuscles may be diminished in number with either a diminished, normal, or perhaps an increased percentage of hemoglobin.

The important diagnostic points observed in 20 cases were: (1) the high color index; (2) the severe degree of poikilocytosis; (3) the constant presence of polychromatophilia; (4) the number of megaloblasts, usually predominating over the normoblasts. The writer considers these points to be pathognomonic of the disease. Billings (Amer. Jour. Med. Sci., Nov., 1900).

Of all the morbid changes which occur in the blood, the most important is the presence of megaloblasts. In 29 cases of the malady observed by the author, only in 1 could these large corpuscles not be found on repeated examination; in the remaining 28 they were present, and in the majority of instances could be detected on the first examination. Naegeli (Wiener med. Woch., Aug. 22, 1903).

Leucocythemia.—This disease may be excluded by the absence of the characteristic blood-change: excess of white corpuscles.

Pseudoleucocythemia is excluded by the absence of the affection of the lymphatic glands which characterizes this disease, more commonly known as Hodgkin's disease.

Leukemia.—In leukemia the patient often does not show enough pallor to make the physician suspect the disease. The lips have a dirty-red color rather than a peculiar pallor. The number of white corpuscles would cause pallor in

a patient with simple anemia, but in this disease the opacity of the blood is great and the pallor fails to show (Janeway).

Gastric Cancer.—This condition almost always shows itself after the age of 40 years, whereas pernicious anemia is generally observed early in life. In cancer the skin is pale; in pernicious anemia the peculiar lemon color is striking in the majority of cases. While gastric symptoms and absence of hydrochloric acid are prominent features of cancer, the digestive disorder is slightly marked in anemia and examination of the gastric contents is negative.

> The reduction of red cells is greater in pernicious anemia than in cancer. The reduction of hemoglobin relative to corpuscles is not so great in pernicious anemia as in cancer. The average size of red cells is greater and polychromatophilia is marked in pernicious anemia. In cancer the cells are small and may show fissures, but not so marked polychromatophilia. Megaloblasts are present generally in greater numbers than normoblasts in pernicious anemia; their mere presence is of great importance, as, although normoblasts are common, megaloblasts occur with very great rarity in cancer. In the absence of complication there is no leucocytosis, and in the absence of fever there is lymphocytosis in pernicious anemia. In cancer leucocytosis is the rule; lymphocytosis does not occur. The author refers to four groups of cases, and in each group the blood characteristics have something in common: acute favorable cases; chronic cases; subacute cases; acute unfavorable cases. Alexander Goodall (Scottish Med. and Surg. Jour., April, 1902).
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> The value of laboratory methods in the differential diagnosis of pernicious anemia and cancer of the stomach is illustrated by the case of a man 50 years of age who had been regarded as a case of gastric cancer by other physicians until his blood had been carefully examined. In such cases when megaloblasts are found in the blood we have a positive diagnosis of pernicious anemia, while if there is cancer of the stomach the principal feature of the blood is a marked leucocytosis. Cerconi (Riforma medica, July 6, 1907).

Finally, increasing emaciation attends a cancerous disorder, whereas in cases of pernicious anemia the patient not only retains his adipose tissues, but sometimes becomes corpulent. In rare cases, however, there has been extreme emaciation.

> Is it possible to diagnose pernicious anemia by the early symptoms before the appearance of the characteristic blood-picture of the disease? While the literature shows that there is no regularity in the order of their appearance, there are facts enough to indicate their importance. In the writer's 20 cases, achylia gastrica, with its associated diarrhea, was present in 14, and in 9 it was a very early symptom. In one case it seemed to have been present thirty-five years before the blood condition was recognized, and in another it was present eight years before the blood-picture developed; in still another case reported it was present six years before.
>
> The nervous phenomena may occur early or late, and in only 1 of his 6 cases with early nervous symptoms did they appear before the signs in the blood were found. The cardiovascular are the least characteristic early symptoms; in only 1 of his 5 cases presenting them as such did he properly interpret them before finding the pathognomonic blood signs. The author, therefore, is unable at present to describe a symptom-complex indicating pernicious anemia before the occurrence, or discovery, of the blood changes, but he believes, nevertheless, that a more careful study of patients in the early stages of the disease will give considerable evidence that such a symptom-complex exists. J. A. Lichty (Jour. Amer. Med. Assoc., June 29, 1907).

The pernicious anemia of infants—a rare condition—is recognized, according to Rotch and Ladd, through the following diagnostic points: The insidious onset with moderate and paroxysmal attacks of indigestion, the extreme pallor, great loss of strength, slightly elevated temperature for months, and absence of glandular or splenic enlargement or of any demonstrable cause for a secondary anemia. The signs which are almost pathognomonic in adults lose significance, on account of the greater instability of the infant's blood-making function. Megaloblasts, normoblasts, macrocytes, and poikilocytes may occur in grave anemia as other than "pernicious"; still, these elements are needed for diagnosis.

ETIOLOGY.—The main pathogenic factor, hemolysis, has been reviewed under a preceding heading; we still have to consider, however, the conditions which either predispose to the disease or are capable of causing it.

As to predisposing agencies, although the disease occasionally occurs in children, it is most common in adults between the ages of 20 and 40 years. Males are attacked more frequently than females, with a slight difference in favor of the former. The disease is more prevalent among the better than in the lower classes, and is most common in Europe, especially in Switzerland, *e.g.*, in regions in which the people are badly fed and live in poorly ventilated and badly lighted houses. Fright and grief are prominent etiological factors. Syphilis, sarcoma, and other disorders capable of impairing hematopoietic functions of the bones are also capable of bringing on the disease.

According to Grawitz, the following group of etiological factors has been established: 1. Gastrointestinal disease of long standing, poor food, impaired digestion; chronic constipation, especially in women frequently pregnant; irregular defecation in women and girls, especially those of hysterical temperament. In such cases it is due to intoxication from the gastrointestinal tract. 2. Pregnancy. Here, too, probably, there is an autointoxication from the intestinal tract, on account of pressure exerted by the gravid uterus on the bowel. 3. Chronic hemorrhages, especially of small size. 4. Constitutional syphilis, particularly when associated with sclerosis of the marrow of the long bones. 5. Bad hygienic conditions of various kinds, especially in the female sex; hard work, with insufficient food, bad air, and emotional excitement. In higher social strata the disease may be found in women who are subjected to intense mental strain as the result of a desire to equal men in physical efforts. Frequent pregnancy and prolonged lactation are also factors. 6. Chronic poisoning, as, *e.g.*, by carbon monoxide. 7. Bothriocephalus and ankylostomum—those cases belong here that are not cured after the expulsion of the worms.

> Variations in nitrogenous metabolism of 21 cases of bothriocephalus anemia studied at the Helsingfors medical clinic. In all cases there was a distinct nitrogen loss up to 8.8 grams per day before the worm was expelled. Afterward the nitrogenous balance was at once or by degrees entirely regained. In some cases there was retention of nitrogen. The writer ascribes the increased nitrogen output to the action of a toxin produced by the worm upon albuminous matter. No parallel was found between the blood conditions and the nitrogenous excretion. With a purin-free diet the urinary purin excretion showed marked variations. During the toxic period—that is to say,

while the worm was present in the intestines—the endogenous purin excretion was very large. When the worm has been removed, the quantity of purin excreted sank rapidly to the normal. In some cases, however, it continued high for some days after the expulsion of the worm. The toxins secreted by the worm evidently incite leucocytosis to a high degree, and also extensive destruction of nuclear matter. E. Rosengrist (Zeit. f. klin. Med., Bd. xlix, 1903).

Pernicious anemia is not a specific entity, but a clinical syndrome of varying etiology. Etiologically, the disease can be considered as cryptogenetic, or of concealed origin. Under the former the writers group: (1) repeated hemorrhage (gastric, uterine, nasal, and vesical); (2) intestinal parasites (bothriocephalus and ankylostoma); (3) malaria; (4) bacterial infections; (5) tuberculosis; (6) syphilis; (7) cancer, especially gastric; (8) gastrointestinal disorders and autointoxications, which are said to be the cause of the so-called idiopathic cases; (9) nephritis; (10) pregnancy; (11) lead; (12) carbon monoxide, arsenic, and opium. The factors necessary for any of the above conditions to result in this syndrome are (*a*) an excessive intensity of the morbid cause; (*b*) the localization of the infection; (*c*) the duration or repetition of the cause; (*d*) an accumulation of the morbid condition; (*e*) predisposition. On the whole, progressive pernicious anemia can be the final stage of secondary anemias. Ladd and Salomon (Revue de méd., April and May, 1908).

Three cases of severe anemia witnessed due to repeated small bleedings and occasionally larger ones from varicosities situated 10 to 15 cm. above the anus which could easily be seen with the proctoscope. Destruction of these varicosities by the Paquelin cautery rapidly cured the anemia. C. A. Ewald (Berl. klin. Woch., Jan. 9, 1911).

Pregnant women represent the largest proportion of cases. Repeated parturition is probably the most prolific cause of the disease, for it is seldom met with in primiparæ. Excessive and prolonged lactation and puerperal hemorrhages and other exhausting conditions frequently appear as the primary element in the causation of the disease.

Certain atrophic conditions of the gastric mucous membrane, ulcers of the stomach, malaria, syphilis, cancer, and alcoholism have also been considered as etiological factors.

PROGNOSIS.—Although the disease terminates fatally when left to itself, the mortality from very nearly 100 per cent. has been reduced since the introduction of arsenic. A guarded prognosis should always be given, however, relapses being exceedingly common. About one-half of the fatal cases last from one to six months; the remaining seldom reach beyond the second year. Periods of transitory improvement of varying duration are often a part of the natural course of the disease; so that too much importance must not be attached to the favorable results that may follow the special line of medication employed. Even if such improvement continues for a long time, the conclusion must not be too hastily reached that the disease is cured. According to Goodall, the prognosis may to a certain extent be based upon certain characteristics of the course of the blood-picture:—

1. **Acute Favorable Cases.**—In these the symptoms are marked; the red cells are much diminished, but show a tendency to rise; the megaloblasts are atypical and not numerous; the normoblasts are numerous; the color index is high, but tends to fall; the polychromatophilia is not marked; the percentage of polymorphonuclear cells is high; the myelocytes are absent or scanty.

Course.—A remission to a fairly normal condition may occur, which may be maintained for years.

2. **Chronic Cases.**—In these the symptoms are not well marked; the red cells tend to remain about one or two million; the megaloblasts are absent or scanty; the normoblasts are absent or scanty; the color index is generally low; the polychromatophilia is slight; the percentage of lymphocytes is high; the myelocytes are scanty.

Course.—The cases are apt to be chronic. The patients can work, though they feel weak, and, though febrile attacks, etc., may occur, they have little bad effect. The improvement seldom occurs, but the duration may be for several years.

3. **Subacute Cases.**—In these the symptoms are fairly well marked; the red cells about one million, showing slow and irregular tendency to rise; the megaloblasts are numerous; the normoblasts are less numerous than megaloblasts; the color index is high; the polychromatophilia is distinct; the percentage of lymphocytes is high in the absence of fever; the myelocytes are fairly numerous.

Course.—Symptoms improve; blood improves to a certain extent. The duration is about two years, unless complications reduce this period.

4. **Acute Unfavorable Cases.**—In this type the symptoms are marked, and there may be hemorrhages; the red cells are about one million, and tend to remain or go lower; the megaloblasts are typical and numerous; the normoblasts are less numerous than megaloblasts; the color index is high; the polychromatophilia is marked; the percentage of lymphocytes is high in the absence of fever; the myelocytes may be numerous.

Course.—A fatal termination is to be expected in a few months.

With improvement of blood conditions improvement of the general health by no means always follows. Patients with pernicious anemia do not always die of the anemia itself, for many cases with abnormally low hemoglobin and blood-count improve. They die more frequently of the secondary organic changes caused by the anemia, chief among which are fatty degeneration of the heart muscle and functional disorders of the nervous system. The prognosis is, therefore, not alone dependent upon the blood conditions, but also upon that of the other organs. Conclusions from the blood alone can lead to great error in the prognosis. Hirschfeld (Therapie der Gegenwart, Nu. 8, 1907).

The tendency to relapse is in reality due to the remarkable persistence of the specific hemolytic infection underlying the disease, since it is always accompanied by a recrudescence of the lesions in the tongue, stomach, or intestine, and by the glossitic, gastric, or intestinal symptoms connected therewith. Hunter (Brit. Med. Jour., Nov. 9, 1907).

The immediate prognosis in certain cases of pernicious anemia with blood depletion below 400,000, although serious, is not hopeless. The prognosis depends on the degree of red-cell regeneration in the bone-marrow, the age of the individual and the potency of the hemolytic poison being important factors. Stone (Jour. Amer. Med. Assoc., April 18, 1908).

Report of 3 cases of pernicious anemia with remissions, with tabulated blood-counts. In one case the improvement followed the removal of the patient from the county farm to the hospital, where the better hygienic and dietary conditions were undoubtedly a strong factor. In several cases observed, out of a total of 25 in the last two and a half years, in which fermentative changes in the intestines were a prominent symptom, high colonic irrigations with physiological salt solution

seemed to be connected with remissions of improvement. Though the blood-count shows a marked improvement in the remissions, there are still abnormal features indicating that a disturbance in hematogenic function still exists. At best a remission is but a partial cure, and reserve in prognosis and caution in interpreting apparent therapeutic results are always advisable. W. L. Bierring (Jour. Amer. Med. Assoc., Aug. 1, 1908).

Case of pernicious anemia in which there was a period of complete remission of symptoms, amounting to a cure for some sixteen years, with final relapse showing all the characteristic symptoms and pursuing a truly progressive course to a fatal ending. A. McPhedran (Amer. Jour. Med. Sci., Aug., 1910).

TREATMENT.—Arsenic cures the curable cases and benefits the others. Iron is worse than useless, having shown itself injurious in several cases reported—doubtless because the liver is already overladen with iron. Fowler's solution may be given in 3-minim doses three times a day, increased by 1 minim daily until 30 minims are taken after each meal, provided the stomach does not rebel, which is seldom the case. The patient should be watched and the drug reduced or discontinued temporarily on the appearance of any of the physiological effects of arsenic: edema of the lids, etc. In some instances the doses have been increased with marked benefit until as much as 20 drops were taken at a dose.

According to Grawitz, **rest in bed** is one of the first requisites; the assimilation of food must be stimulated. The patient should be placed on a milk and vegetable **diet. Lavage of the stomach, intestinal irrigation,** and **saline laxatives** are useful. If the urine contains much indican **intestinal antiseptics** are indicated. He also regards **arsenic** as the best remedy; it can be given with **quinine.** Inhalations of **oxygen** have been employed with advantage. **Massage** and **gymnastic exercises** are often of service. After apparent recovery the patient must be carefully observed, as relapses are likely to occur, particularly if the hygienic and dietetic conditions are unfavorable.

Case of pernicious anemia treated by Grawitz's method. The patient was a man 33 years old who was admitted to the hospital after suffering for five weeks from anemia and weakness. All the symptoms manifested by the patient were that of a typical case of pernicious anemia. Treatment consisted of a strict **diet** of milk and vegetables, daily **enemata,** with **arsenic** and **hydrochloric acid** given by the mouth. Lavage of the stomach was not performed, owing to the strenuous objections on the part of the patient. After eight weeks in the hospital and a month's holiday in the mountains his general condition was excellent, and there has been no relapse. The adventitious sounds which had been heard over the heart and cervical veins had disappeared. He no longer felt dyspnea on slight exertion, the temperature became normal, and the pulse was 68-80. The blood-count showed 4,235,000 red cells and no abnormal cells, as compared with 1,300,000 red cells and numerous microcytes and megalocytes and a marked poikilocytosis and polychromatophilia on admission to the hospital. The success obtained in this and similar cases tends to confirm the view that the disease is toxemia, caused by a deficiency of hydrochloric acid in the gastric juice and a possibly subsequent splitting up of albuminous molecules into toxic bodies rather than to a primary disease of the blood or blood-forming organs. L. Nicolayson (Lancet, Nov. 7, 1908).

Experiments based on the hemolytic action of distilled water show that arsenious acid forms a fixed combination with red blood-cells and acts as a protective agent against hemolytic agen-

cies. The protective action of arsenic was perceptible when the experimental solution was as weak as 1:400,000. The ordinary maximum dose of arsenic is 0.005 gram, and if this was all absorbed the amount of arsenic in the blood would be 1:1,000,000. However, arsenic is frequently given in larger doses in the organic combinations, and it is very slowly eliminated. Furthermore, arsenic seems to attach itself so rapidly and so firmly to the red blood-cells that it is probable that the drug is largely taken up by them. Therefore, the writer believes that arsenic is of benefit in pernicious anemia because it prevents the destruction of the red blood-cells, and that arsenic protects the red blood-cells from invasion by the malarial parasite, but that it does not destroy the parasite. Gunn (Brit. Med. Jour., No. 2481, p. 145, 1908).

When the gastric disorder, which is a usual symptom, prevents the administration of **arsenic**, the latter may be given **subcutaneously**, while the stomach is treated directly by lavage.

An excess of hydrochloric acid is not uncommonly found in the gastric secretions. In such cases Sée recommends an almost exclusive diet of meat and other albuminous foods: **raw meat** to the extent of 10 to 12 ounces daily. As a rule, however, there is deficiency of hydrochloric acid and pepsin, especially in advanced cases. Good effects have been obtained from large doses of **hydrochloric acid** and **pepsin** under these conditions.

The great majority of cases of pernicious anemia suffer from an absence of hydrochloric acid and pepsin in the gastric secretion, and this condition is further harmful in that the essential element for pancreatic secretion is produced only under the stimulus of the acid chyme passing over the duodenal mucosa. To cause an artificial digestion, pancreatic as well as gastric, hydrochloric acid and pepsin in much larger doses than are usually considered permissible prove effective. In a personal case, the patient received 30 grains of **pepsin** and 105 minims of dilute **hydrochloric acid** three times a day, the latter being given in 15-minim doses every ten minutes in albumin water to disguise the taste. The fact that the acid was given combined instead of free did not affect its action. The further treatment consisted in daily **irrigations of the colon** and a liberal **mixed diet.** It was shown from the blood examination that the treatment had been followed by most satisfactory results. Julius Rudisch (Med. Rec., March 5, 1910).

The use of **bone-marrow**, introduced by Fraser, has given good results in some cases and no results whatever in others. Freshly prepared each day with an equal quantity of glycerin, red marrow, 1 or 2 ounces daily, has seemed to give the best results. It should be tried only where arsenic has failed.

Transfusion of blood should never be omitted when improvement does not follow the administration of arsenic. The best method is that employed by Brakenridge, of Edinburgh. The blood is kept fluid by admixture with one-third part of its bulk of a 1:20 (5 per cent.) solution of phosphate of soda in distilled water kept at blood heat. John Duncan, who performed the transfusions in Brakenridge's cases, insists upon the necessity of slowness in operating. He regards thirty minutes as the minimum time that should be occupied in injecting 8 ounces of the fluid.

Case in which such a rapid transformation in the general condition and in the blood-picture followed the **transfusion of blood** that it is impossible to ascribe the phenomena observed to a mere coincidence. The technique was as follows: Injection of about 325 Gm. of defibrinated blood

into the median vein of the patient, about 250 c.c. actually entering the vein. There was no disturbance at the time, but a chill occurred in thirty minutes with transient rise in temperature. The improvement commenced the next day and the curves appended showed the transformation, the hemoglobin running up to 75 per cent. and the reds from 985,000 to 3,720,000 in one month. The principal danger from therapeutic transfusion of blood lies in the loss of vitality of the red corpuscles. They die if they are heated too much; consequently the blood to be injected must never be warmed over 45° C. They also die if they remain too long outside the body, although they may be kept on ice up to seventy-two hours. If blood is used from persons requiring therapeutic venesection on account of eclampsia, uremia, or edema of the lungs, there is a possibility that such blood may prove injurious, and there is also a possibility of transmission of constitutional disease. As the fibrin-ferment is released by the destruction of white corpuscles, blood unusually rich in leucocytes should never be used for transfusion. Sachs (Zeit. f. Geburts. u. Gynäk., Bd. lxiv, Nu. 2, 1909).

Seven cases in which threatening anemia was benefited to a remarkable extent by **transfusion** of only 5 c.c. **of human blood.** The transfusion of this small amount is simple and generally harmless, but in a few cases there were signs of mild disturbances after the transfusion. It seems as if the blood from certain persons displays more toxicity than from others, 3 patients injected with a certain blood all presenting the same transient disturbances. It was never noticed that when two or more patients received blood from the same source the one presented disturbance and the other did not. A. Weber (Deut. Archiv f. klin. Med., Sept. 4, 1909).

No actual progress has been realized of late in treatment of pernicious anemia. The trouble is seldom recognized early enough for effectual treatment, but the writer's experience with 4 cases seems to confirm the possible benefit from transfusion of small amounts of defibrinated blood injected into the gluteal muscles. The writer obtained very favorable results from such injections. The first patient was a woman teacher with symptoms of severe pernicious anemia for three years. After 14 injections of 10 or 20 and up to 50 c.c. of blood in the course of eleven weeks, the reds increased from 1,200,000 to 4,500,000 and the hemoglobin from 18 to 92 per cent. The benefit was equally striking in the case of a man of 41, given 9 injections in less than three months, the reds increasing to 5,200,000. In a young girl with ordinary anemia and chlorosis the hemoglobin increased from 40 to 75 per cent. and the reds from 3,200,000 to 4,800,000. The blood injected subcutaneously does not pass directly into the circulation and is still evident four or five days later at the point, the reds still retaining largely their normal shape and staining properties, but the hemoglobin probably lakes out into the circulation and thus aids in restoring normal conditions in the general blood-supply, or the injected blood may provide certain other substances lacking in pernicious anemia. The injections do not act on the cause of the anemia, and arsenic is needed for this. By-effects were rare and slight, merely occasional painfulness at the point of injection. Huber (Deut. med. Woch., June 9, 1910).

Three cases in which **transfusion of blood** was resorted to. The transfusion proper occupied an hour or more, as a rule. During that time the appearance of death-like pallor which these patients presented changed to that of comparative health. The color first reappeared in the cheeks and tongue and then mounted into the lips, the conjunctivæ, and the skin generally. The hemoglobin can easily be followed, and in Dare's or Fleischl's instrument showed a steadily increasing percentage. In the 2 favorable cases this amounted to an increase of three or four times the original percentage.

There was a corresponding change in the patient's mental condition and vitality, which seems, in patients so near to death, almost miraculous. This was strikingly true in the first case. In both favorable cases the transfusion introduced a period of improvement which in the first case has now lasted nine months; in the third, two. The hemoglobin and the number of red cells have increased steadily until 80 per cent. and more has been attained. Bovaird (Med. Record, Feb. 11, 1911).

Defibrinated blood has been used **subcutaneously** by Westphalen with success.

Subcutaneous injections of **normal saline solution** every alternate day, and on the intervening **saline enemata,** with **arsenic** internally, have been recommended by McPhedran.

Intestinal antiseptics have been recommended. Hunter holds that the best intestinal antiseptic is **betanaphthol** and **salol,** along with **arsenic** when that can be borne. I consider **thymol** entitled to the first position, a fact which seems to be more fully appreciated in Italy than elsewhere. In accordance with the view that pernicious anemia is due to the absorption from the intestine of substances foreign to the healthy body, and destructive to the red corpuscles, its treatment by intestinal antiseptics is certainly most rational.

When the disease is due to the *Ankylostoma duodenale,* **thymol,** 2 to 3 drams daily, is a very effective vermicide, according to Bozzolo.

Two cases due to *Bothriocephalus latus,* the infection being accompanied by the severest kind of anemia. In one patient the red corpuscles fell to 780,000 and the hemoglobin to 15 per cent. The second case was even more severe, the red corpuscles falling to 660,000 and the hemoglobin to 10 per cent. Hemorrhages were noted along the veins of the retina. The improvement in both cases after **thymol** treatment was marvelous, and in the second patient in thirteen days the number of red corpuscles trebled. A. Meyer (Med. News, April 8, 1905).

Serum therapy seems to merit further trial, though not much more than temporary benefit can be expected from its use.

Antistreptococcic serum used with gratifying results in 2 cases of anemia: one pernicious, the other simple. In the former, examination of the blood showed 4000 white and less than 1,000,000 red corpuscles to the cubic centimeter, and 30 per cent. of hemoglobin. Eight injections of 8 c.c. each were given at intervals of two or three days. After the third, improvement began and progressed steadily. Three days after the last injection the blood contained 5000 white and 4,960,000 red corpuscles, and 90 per cent. of hemoglobin. W. H. de Witt (Cin. Lancet-Clinic, lxxxiv, p. 61, 1900).

Typical case in a man 37 years of age. The treatment consisted of oral and gastric antisepsis. During July three injections of antistreptococcic serum were given. After the first the red corpuscles rose to 36 per cent.; after the second to 52 per cent., and in three weeks the red corpuscles rose to 65 per cent. and the hemoglobin to 72 per cent. In September arsenic was added to the other treatment, and by December the red corpuscles had risen to 94 per cent. and the hemoglobin to 100 per cent. William Hunter (Lancet, March 30, 1901).

Herter recommends frequent and thorough **irrigation of the colon,** since it is the chief thriving place of the anaërobic bacteria which cause the specific putrefaction. Following this suggestion, Dittmar and Hollis were able to report a few months ago recovery in 2 cases of pernicious anemia by irrigation of the colon which had resisted all other methods of treatment.

In all cases of pernicious anemia, the stools should be examined to determine the presence of a *Bacillus capsulatus aërogenes* infection. If these bacteria are present in great quantities, then **high irrigation**, combined with **arsenic** internally, should be used; and if the patient fails to improve, then the appendix offers the best route for thorough irrigation. Lucius E. Burch (Jour. Amer. Med. Assoc., March 13, 1909).

When the *Bacillus capsulatus aërogenes* or the percentage of anaërobic bacteria found in evacuations from bowels is large, then, after thorough trial at colonic irrigation and failure to improve the symptoms or to lessen the percentage of bacteria, the operation of **appendicostomy** is warranted. J. A. Witherspoon (Southern Med. Jour., July, 1909).

Cholesterin has been introduced into the therapy of pernicious anemia because of Ransom's finding that it prevented the hemolytic effects of some substances, such as saponin and cobra poison. A 3 per cent. solution of cholesterin in oil is given in 100-Gm. (3⅓ ounces) doses daily. It is apt, however, to disagree with the patient.

The objections to the use of **cholesterin** consist mainly in the fact that this substance is not at all decreased in the blood of the patients, but is often increased above the normal figures. Cholesterin in 3 per cent. solution in oil was given by the writer, but this disagreed with most patients. The feeding of milk, cream, and butter, however, accomplishes the same results by increasing the fat and the cholesterin contents in the blood. Large amounts of these substances were used in the diet, and the results were very favorable, though it is impossible to say whether the cholesterin had anything to do with it. **Arsenical preparations** were also given. Klemperer (Berl. klin. Woch., Nu. 52, 1908).

Cholesterin tried in 6 typical cases of cryptogenetic pernicious anemia, one of them being of the so-called aplastic type. Three patients were in an advanced state of the disease when coming under observation and only lived for a few weeks; in these no effect whatever was observed from the use of the cholesterin. A fourth patient was discharged unimproved after a three weeks' course of the treatment and died a few days later. In the fifth only 24 Gm. had been administered when the treatment was suspended, and death occurred shortly thereafter.

An apparently beneficial effect was obtained in the remaining case, but, as the patient at the time when the cholesterin treatment was begun was virtually in her first attack, one naturally hesitates to ascribe the noted improvement to any one therapeutic factor. It is noteworthy, however, that the resumption of the cholesterin some months later, when a relapse had occurred, was again followed by marked improvement. This patient is still living and in good condition. When first seen the red cells numbered 1,744,000, while the hemoglobin was 46 per cent.; there was then marked anisocytosis with a distinct tendency to macrocytosis; there were poikilocytosis and extensive granular degeneration (so-called). C. E. Simon (Jour. Amer. Med. Assoc., Dec. 19, 1908).

Three cases of pernicious anemia and 1 of secondary anemia referable to nephritis in which **cholesterin** was used for therapeutic purposes, the aim being to counteract any hemolysins that might be active in a manner analogous to the action of cholesterin on cobra lecithide. Of the 3 cases, one patient remained unimproved, while in the other two cholesterin was decidedly beneficial. The latter case was in a wretched condition, with intense dyspnea, ascites, pleural effusion, edema, and a red count of 750,000 with 18 per cent. of hemoglobin. After a week the count had risen to 1,750,000 and the hemoglobin to 30 per cent., while the threatening symptoms had all disappeared. The improvement was thus quite remarkable, but after a few weeks no further

gain was obtained and still later a relapse occurred which ended fatally. Reicher (Berl. klin. Woch., Nu. 41-42, 1908).

Glycerin has also been tried in parasitic pernicious anemia, as a result of Tallquist and Faust's suggestion that glycerin might combine with the lipoid substance assumed to be responsible for the disintegration of the red corpuscles and thus combine to form a harmless product. The special lipoid substance found in the anemia from intestinal parasites proved to be oleic acid, and this combines with glycerin to form triolein.

In the first of 2 cases in which **glycerin** was tried, the result was very encouraging, and in the second administration of 3 tablespoonfuls of glycerin a day, with lemon juice, was followed in the course of two and a half months by an increase in the red corpuscles from 990,000 to 4,760,000, and of hemoglobin from 20 to 90 per cent. No other drugs were given, except a little antipyrin and caffeine, for a day or so to combat a neuralgic headache. Vetlesen (Norsk Mag. f. Laeger, Oct., 1909).

Case in which there were only 970,000 red and 4000 whites, with 20 per cent. hemoglobin. Death seemed imminent when a tablespoonful of **glycerin** was given three times a day at first, and later up to 70 Gm. The man, a syphilitic in whom the iodides and mercury had been tried, began to improve at once and by the end of a month the reds numbered 4,200,000, the whites 5300, with 100 per cent. hemoglobin. This confirms Tallquist's experience in a similar case. Both patients seem to be permanently cured.

The writer's patient is still taking glycerin, but is strong and well. Muktedir (Deut. med. Woch., May 18, 1911).

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ANEMIA, SECONDARY, OR SYMPTOMATIC.— DEFINITION.—A deficiency either in the quantity or the quality of the blood, affecting the blood mass or the cellular and albuminous constituents. Genuine secondary anemia is essentially a symptomatic disorder, referable to obvious pathological conditions, which deplete the blood volume, diminish the number of erythrocytes, and reduce the amount of hemoglobin and albumin.

["Anemia," "Primary" or "Idiopathic Anemia" are now obsolete as designations, all anemias being, in the light of modern research, due to some underlying cause—though many of these are still undetermined—and therefore "secondary" or "symptomatic." Hence the above heading and definition. The EDITORS.]

TYPES OF SECONDARY ANEMIA.—It is convenient to classify the simple secondary anemias into several clinical groups which relate directly to the predominant factor active in the individual case. While a classification of this sort must needs be imperfect, for frequently several factors are concerned in a single instance, it will serve to designate the important underlying condition of which the blood impoverishment is symptomatic. The following groups are sufficient for the inclusion of all anemias of secondary origin: I, posthemorrhagic; II, infectious and toxic, and, III, trophic.

I. **Posthemorrhagic anemias** comprise that varied class of cases directly traceable to bleeding, irrespective of its extent, duration, and character. In this group, therefore, are included the acute anemias due to loss of blood by trauma, operation, abortion, parturition, epistaxis, hemoptysis, gastric and intestinal ulcer and neoplasm,

hemorrhagic pancreatitis, and under the same heading are the grave anemias consecutive to the rupture of an aneurism, of a Fallopian tube, and of a large mass of varicose veins. The hemorrhagic diseases (purpura, hemophilia, scurvy), hemorrhoids, and uterine fibroids, all of which are capable of causing persistent, though perhaps moderate, loss of blood, may also excite a secondary anemia, perhaps of pronounced severity.

II. **Infectious and toxic anemias** develop chiefly as the result of hemolytic agencies, and are encountered in the specific infections, malignant disease, intestinal helminthiasis; in poisoning by certain so-called blood poisons—nitrobenzol, potassium chlorate, lead, mercury, arsenic, antimony; and in states of autointoxication—uremia, cholemia, pregnancy. Of the acute febrile infections that account for anemia of moderate intensity, enteric fever, sepsis, variola, erysipelas, rheumatic fever, and scarlatina may be named as typical examples. The anemia excited by malignant neoplasms is attributable partly to the action of circulating tumor-toxins and partly to concomitant factors, such as hemorrhage, ulceration, and interference with nutrition, as in esophageal and gastric growths. The anemia of helminthiasis is due principally to the hemolytic action of poisonous substances elaborated by the worm, notably in the case of uncinariasis and bothriocephalus disease, and to a less extent in persons harboring oxyurides, ascarides, and filariæ. Helminthiasis anemia is also favored by the associated gastrointestinal disorders, and, in uncinariasis, the parasites suck blood from the intestinal vessels of the host and pour out an absorbable anticoagulant material which may act deleteriously upon the circulating blood-cells. The luetic virus materially damages the hemoglobin and erythrocytes, and syphilitics as a class are subject to a form of toxic anemia which as a rule attains its greatest development during the tertiary stage of the infection. In malarial fever it is probable that the presence of a circulating specific malarial toxin, produced by myriads of parasites, has much to do with provoking the attendant anemia, and it is certain that in this infection the blood must suffer from the wholesale destruction of parasitiferous erythrocytes.

> There is a type of apparent anemia which is often mistaken for real chlorosis, until an examination of the blood shows that the number of red corpuscles and the percentage of hemoglobin are normal. In such cases the writer thinks a history of past or present tuberculous disease can always be found. This condition was recognized by Trousseau, and was called by him "false chlorosis" or "tuberculous anemia." Several cases of this condition are cited in detail. In treatment, iron is to be avoided, and open air and hygiene are important. A. James (Brit. Med. Jour., Dec. 28, 1907).
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> Insufficiency of the blood-forming function is not, primarily at least, at fault in the production of the secondary anemias following chronic gastrointestinal disease. The writer considers the anemia more probably due to the existence in the blood-serum of hemolytic substances, perhaps produced by chemical changes connected with functional disturbances in the digestive organs. Besides the indirect pathological evidence of the existence of such hemolytic action, the writer has been able to demonstrate it directly by the action of the serum of anemic rabbits on the blood of normal ones. With its globulicidal power it has a certain stimulant

action on the blood-forming apparatus in the bone-marrow, which, however, seems to be more quickly exhausted than is its destructive action. The author considers that his study emphasizes the importance of functional over anatomical gastric lesions in the production of anemia. Tixier (Semaine méd., June 19, 1907).

Cultures of dysentery, colon, and typhoid bacilli grown upon agar suspended in salt solution and then extracted with alcohol at 37° C.; these extracts were found to have a slight hemolytic power for dogs' blood *in vitro*. When injected into rabbits these extracts produced a distinct, but moderate anemia. An attempt was then made to increase the hemolytic activity of these organisms by enhancing their virulence. For this purpose irritation of the gastrointestinal tract was brought about in dogs and rabbits by means of chemicals, and later large quantities of cultures of the organisms were introduced into the stomach. Twenty-four to forty-eight hours after the intestinal infection had been set up the animals were killed and the organisms recovered again from the intestinal tract. Extracts of the organisms which had caused these intestinal infections were found to have increased considerably in hemolytic activity *in vitro*. When the extracts were inoculated into dogs and rabbits a marked and rapid anemia developed, with reduction in both hemoglobin and red corpuscles. Fejes (Deut. Arch. f. klin. Med., Bd. cii, S. 129, 1911).

III. **Trophic anemias,** or those of nutritional origin, are met with commonly in subjects that suffer from chronic malnutrition due to faults in the quantity and quality of their food, to defective absorption and assimilation, or to a combination of these two causes, and in many such instances deficient air and sunshine, lack of exercise, confining occupation, and unsanitary surroundings must likewise be reckoned with as contributing elements. Drains upon the albumins of the system, as in habitual nephritis, persistent suppuration, prolonged lactation, and chronic dysentery, ultimately provoke well-defined, stubborn anemia of the trophic type.

Congenital anemia is sometimes due to heredity. Habitual anemia of the parents, cachexia as a result of tuberculosis, malignant neoplasms, diseases during pregnancy, poor nutrition and lack of hygiene, may all, according to the author, give rise to anemia in the child. The anemia is transmitted by means of the placental circulation and continues to develop in the fetus *in utero*. The alimentary form when present in the non-anemic newborn is due to an exclusive milk-diet which in itself is deficient in iron. L. Fürst (Therap. Monats., Nu. 9, 1900).

An anemia is often observed in young children that is due to improper feeding. This may consist of carelessly prepared artificial food, bad quality of milk, irregularity of feedings, the use of too large quantities of food, the use of solid food before the age of 9 months, stimulating drinks, insufficient nursing, brutal weaning, and the abuse of milk after weaning. The writer believes that this form of anemia is more frequent in young children than the anemia of tuberculosis, of syphilis, of malaria, or of lymphadenia. Rougier (Paris Thesis, No. 13, 1901-1902; Gaz. heb. de méd. et de chir., Feb. 9, 1902).

In patients with insufficient or absent secretion of gastric juice there is always evidence of anemia. In hyperacidity the hemoglobin was found above normal, and in nervous dyspepsia it was practically normal. Only in the cases ranging from subacid gastritis to gastric achylia was anemia the constant finding. The writer's experience further demonstrated that administration of natural gastric juice from the dog, supplying the missing element for gastric digestion, was followed by the subsidence of the anemia. The supplementary gastric juice insured proper

nourishment for the elements of the blood. F. Rollin (Berl. klin. Woch., Bd. xliii, Nu. 5, 1904).

In the majority of cases of serious anemia anhematopoiesis is not anatomically demonstrable, and there is usually, if not always, the destruction of the blood which is related to deglobulization. That is to say, in most cases of anemia the study of the anhematopoiesis should not lead one to forget the investigation of the causes of the anemia, the mechanism of the destruction of the blood-globules, which is of great importance from both the pathogenic and therapeutic points of view. C. Aubertin (La semaine méd., July 15, 1908).

In severe anemias experimentally produced the oxidations in the tissues are not carried out completely to the final products of metabolism, but are brought to an end partly in the blood or in other organs. The true cause may therefore be lack of oxygen. Morawitz and Pratt (Münch. med. Woch., Sept. 1, 1908).

The writer refers to the anemia without appreciable cause, and experience has convinced him that these anemic infants are suffering from lack of iron. This form of anemia is more common in families in which the infants are allowed nothing but milk, while it is rare when the children early eat at the family table. He does not give iron directly, but during or after the third month allows once a day a little meat broth with one-half and later the whole yolk of an egg. During the fourth and fifth months gruel is given once or twice a day, made of zwieback with butter, milk, salt, and sugar, to which the egg-yolk is added. By the sixth or ninth month he gives spinach; by the tenth and eleventh months a small amount of meat.

When the child is a year old he reduces the milk to a pint or a pint and one-half a day and accustoms the child to a mixed diet. By this means, the anemia is prevented and always cured when developed. Infants seem to feel the need of iron mostly in the fourth month, and by giving them in this way a little food that contains iron it is possible to keep the hemoglobin at 100 per cent. The children take this diet without disturbance. Yolk of egg and spinach contain 22 and 35 mg. iron in 100 Gm. of dry substance, while cows' milk contains only 2.3 mg. The writer thinks it is not a mere coincidence that none of the children given iron in this way has ever developed rachitis. Milk does not contain enough iron for the proper development of the infant, and sooner or later the child will suffer, especially about the fourth or sixth month, at which time a little mixed food containing iron is given whether the child is getting breast milk or is bottle-fed. J. Katzenstein (Münch. med. Woch., Aug. 10, 1909; Jour Amer. Med. Assoc., Sept. 18, 1909).

PATHOLOGY.—The principal pathologic alterations incident to anemias of the secondary type relate to the composition of the circulating blood and to the histology of the bone-marrow, of which the former changes are the more important, and, obviously, more readily available to the clinician. The blood changes vary within wide limits, depending upon the grade and the chronicity of the individual case; but in general it may be stated that they are of very moderate intensity in the average example of general symptomatic anemia. There is a more or less decided diminution in the number of erythrocytes (*oligocythemia*), with a tolerably proportionate reduction in the percentage of hemoglobin (*oligochromemia*), and, in severe cases, one observes structural changes implicating the erythrocytes' stroma and eventually leading to the production of corpuscular deformities of shape (*poikilocytosis*), and of size (*megalocytosis; microcytosis*). Not always, however, is the hemoglobin-erythrocyte reduction proportionate, for in some forms of secondary anemia the hemoglobin loss is

greatly disproportionate to that of the cells, as, for example, in so-called "syphilitic chlorosis," which, hematologically, counterfeits maiden's chlorosis; on the contrary, in other types the erythrocytes suffer chiefly, as in that variety of parasitic anemia provoked by the *Bothriocephalus latus,* which apes true pernicious anemia in every detail of the blood-picture. These facts call for great caution in attempting to diagnose a secondary anemia by the blood changes alone, without due regard for the discovery of some adequate causal factor to be correlated therewith. In active, severe cases of anemia young, nucleated erythrocytes (*normoblasts*) escape prematurely from the bone-marrow and appear in the circulating blood in limited numbers, and in the event of intense retrograde marrow changes an occasional nucleated corpuscle of fetal type (*megaloblast*) also may be observed. With such evidences of high-grade blood deterioration one also meets with cells disfigured by atypical staining proclivities (*polychromatophilia*), and with cells whose protoplasm is stippled with fine and coarse basic granules (*granular basophilia*), both of which abnormal findings point to a considerable degree of stroma degeneration, whereby the affected cells no longer react toward acid aniline dyes, as they do normally, but show a selective affinity for basic colors, by which the stroma of the healthy red corpuscle is never stained, when exposed to a mixture containing both acid and basic dyes. The behavior of the leucocytes in secondary anemias is most inconstant. In chronic cases, especially those due to trophic defects, and in certain of the slowly progressive toxic anemias the leucocyte count does not deviate from normal, or, if it shows any appreciable change, becomes subnormal (*leucopenia*). In these leucopenic anemias it is also the rule to find a disproportionately high percentage of lymphocytes (*relative lymphocytosis*), these cells increasing in number chiefly at the expense of the polynuclear forms.

The writer using Wright's modification of Leishmann's stain, in studying the blood from cases of anemia, observed peculiar stained ring formations within certain of the red blood-corpuscles. These figures were seen in 3 cases of pernicious anemia, 4 of lead poisoning, and 1 of lymphatic leukemia. Unlike the ordinary basophilic granulations found so often in the red blood-cells from cases of lead poisoning and pernicious anemia, these figures stained not blue, but bright red. The rings were quite perfect. They varied in size: in some instances being very small, in others encircling the extreme periphery of the corpuscle. Rarely they were twisted or had a figure-of-eight form. Occasionally basophilic granulations were noted in the same corpuscle which contained a ring body. Such figures did not appear in blood specimens stained with hematoxylin. The author believes that they may be connected in some manner with cell regeneration, and suggests that they may represent nuclear remains, or, perhaps, portions of the nucleus which have resisted those forces destructive to it, and ultimately to the cell itself. Cabot (Jour. of Med. Research, vol. ix, p. 15, 1903).

Effort to reproduce in the lower animals by repeated bleedings histological changes analogous to those occurring in the aplastic anemia of man. The experiments were carried out upon dogs and rabbits. The dogs were bled daily from a vein, over a considerable period of time; with the rabbits leeches were used to remove the blood. Young animals were found to be suitable for the work because of the rapidity with

which their blood is regenerated after hemorrhage. In older animals, in which the hematopoiesis is less active the bone-marrow showed only slight hyperplasia; this was of the myeloblastic type—the predominating cell being mononuclear and non-granular, nucleated red blood-cells; granulocytes were very few in number. In the spleen megalokaryocytes were found, but no evidences of blood formation were observed here. In one instance the spleen contained numerous phagocytes filled with red cells. No signs of blood formation were observed in the liver. The peripheral blood, which was frequently examined, resembled that seen in aplastic anemia in man in the absence of poikilocytosis and the small number of nucleated red blood-cells, and differed from it in the presence of basophilic granules and polychromatophilia in the red cells, and in the absence of leucopenia and lymphocytosis. The basophilic granules of the erythrocytes the writers look upon as nuclear in origin; the granules were found in the blood of those animals in which regeneration was most active; they were not found in association with aplastic bone-marrow, evidence of their nuclear source. Blumenthal and Morawitz (Deut. Archiv f. klin. Med., Bd. xcii, S. 25, 1907).

Case in which the presence of peculiar red corpuscles was evidently chronic as revealed by the history of the past three years, with yaws and suppurating otitis as predecessors, yet with acute exacerbations. The condition was not clearly explained on the basis of an organic lesion in any one organ. There was cardiac enlargement, albuminuria, and cylindruria, general adenopathy, icterus, with a secondary anemia not remarkable for the great reduction in red corpuscles or hemoglobin, but strikingly atypical in the large number of nucleated red corpuscles of the normoblastic type and in the tendency of the erythrocytes to assume a slender sickle-like shape. The leucocytosis with a rather high eosinophile count was also noted. Syphilis was suggested by many of the facts, such as adenopathy and the conditions of the heart and kidneys; it might explain the anemia, the arthritis and perhaps also the temperature, cough, and attacks of pain resembling hepatic or gall-bladder disease; for, as is well known, visceral syphilis may furnish a most bizarre group of symptoms. The Wassermann test was not in use at this time. The scars said to have been due to yaws were like those left by syphilis. The patient coming from the tropics, one thought of intestinal parasites such as uncinaria as a possible explanation of the anemia and the eosinophilia. What were thought to be eggs were found on one occasion only, and after thymol there was temporary improvement. The odd blood-picture made one examine for possible toxic effects of the coal-tar preparations, but neither from the history nor from the examination of the urine was there any evidence that such drugs were habitually taken. The question of diagnosis, therefore, remains an open one unless reports of other similar cases with the same peculiar blood-picture shall clear up this feature. Herrick (Archives of Intern. Med., Nov., 1910).

Other anemic blood changes, of very minor importance, comprise increased rapidity of clotting and subnormal specific gravity values.

Anemia appearing in the face of active hemorrhage, of acute infectious processes, and of malignant disease is ordinarily attended by a leucocyte increase affecting mainly the polynuclear cells (*polynuclear neutrophile leucocytosis*), and in helminthetic diseases of recent origin there is a very constant increase in the percentage of eosinophile cells (*polynuclear eosinophile leucocytosis*). The presence of small numbers of immature polynuclear neutrophile cells (*myelocytes*) in the blood is frequently noted in many of the severer anemias of symptomatic character, irrespective of the presence or absence of a leucocytosis.

The bone-marrow in a severe case of anemia undergoes a moderate degree of softening and acquires a somewhat reddish hue, the attendant histological changes of this transformation consisting of a hyperplasia of the lymphoid elements and a diminution in the number of fat-cells, which are replaced by marrow-cells or myelocytes charged with neutrophilic and eosinophilic granulations. Nucleated erythrocytes or erythroblasts, chiefly of the normoblastic type, are numerous when active powers of hemogenesis persist. H. C. Bunting's studies of the blood and bone-marrow in rabbits rendered anemic by the injection of hemolytic poisons has thrown a clear light upon the difference between the marrow changes incident to anemias of different grades of development. This investigator showed that hemolytic anemia excited by saponin is associated with more or less effectual depletion of the marrow-centers wherein proliferation of the blood-cells takes place, and with fragmentation and other degenerative changes in the other marrow-cells, the blood-picture betraying this grave myeloid lesion virtually corresponding to that of true pernicious anemia in man. In contrast to these findings, posthemorrhagic anemia, despite the presence of characteristic changes in the peripheral blood, does not affect the integrity of erythrogenic and leucogenic centers of the marrow. Furthermore, it would appear that in some instances the proliferating centers of the marrow become quite replaced by scar tissue, in which event the hematopoietic function, now impossible for the crippled marrow to carry on, is undertaken by the spleen.

There is a well-established relation of diffuse cord degeneration with pernicious anemia. It seems highly probable that the hemolysis and the cord changes are due to the same lesion. While the source of the latter is unknown, the fact that gastrointestinal disturbance is so common in the disease would lead one to suppose that it is of intestinal origin. The diffuse degenerations of the spinal cord which occur in conditions without pernicious anemia do not appear to differ essentially from those of pernicious anemia. It is possible that a common blood-circulating poison exists which may expend its force upon the blood in one individual, upon the nervous apparatus in another, and coincidently upon the blood and spinal cord in others. F. Billings (Boston Med. and Surg. Jour., Sept. 4, 1902).

Examination of a large number of cases proves that the changes in the cord are in a sense mechanically located, that is, those portions of the cord less well supplied with blood are the first to suffer. The posterior half containing the sensory and motor conduction paths is, therefore, more frequently involved, but the gray matter, or even the anterior horns, may be affected. The symptoms are variable and obscure, and may be overlooked; but in some cases they are prominent enough to lead to the diagnosis of tabes, spastic paraplegia, or a neuritis. Symptoms of any of these conditions may be present, depending upon the portion of the cord involved. Almost invariably these patients complain principally of disturbances of sensation. They describe numbness, tingling, and formication, usually in the lower extremities, sometimes in all four. The sensation may be that of pressure from within or without; some feel as if tight bandages were drawn around their limbs. With these sensations there may be a reduction in the reflexes, causing a suspicion of neuritis. There is usually very little atrophy, and the electrical reactions are normal; but sometimes the gray matter of the cord is involved, and both atrophy and elec-

trical changes may be present in the terminal stages. Paralyses, loss of sphincteric action, and marked mental disturbances have been observed, and severe cases usually perish miserably. A. Church (N. Y. Med. Jour., July 26, 1902).

The visceral changes to be noted in cases of chronic secondary anemia include granular degeneration of the liver, kidneys, and heart, and, in some instances, fatty changes in these organs. These lesions depend more upon concomitant disturbances, such as toxemia and nutritional faults, than upon the effect of the anemia *per se*, and it seems within the bounds of reason to assume that they arise in part from an undue visceral activity excited by the organism's attempt to maintain a normal process of oxidation.

Two cases of primary chronic anemia in men of 62 and 68. In this type the anemia is moderate in degree, and is accompanied by enlargement of the spleen, slight poikilocytosis of the red corpuscles, and excessive leucopenia, as low as 660, without essential marrow elements. The affection progresses to a fatal termination in about six months, with variable moderate or high fever of a continuous or intermittent type. The signs of a hemorrhagic diathesis do not appear until late, and are not severe. The bone-marrow becomes completely atrophied or shows signs of acute degeneration. The blood findings are not those of pernicious anemia, especially the leucopenia. The symptoms resembled those of what has been called "aplastic anemia," but the writer thinks that the findings in the bone-marrow were of a different nature. O. Kurpjuwelt (Deut. Archiv f. klin. Med., Bd. lxxxii, Nu. 5-6, 1905).

The liver, the spleen, and frequently the lymph-nodes assume a fetal type in grave or pernicious anemias as far as their cellular character is concerned. Erythroblastic cells and newly formed leucocytes appear in them, while the blood-making organ of the adult, the bone-marrow, shows likewise a picture of greatly increased activity. The writer, together with Heinecke, has interpreted these phenomena as reparative in nature in opposition to another conception of the findings which seeks to interpret them as the primary result of some unknown harmful agent. Von Domarus has greatly strengthened the standpoint maintained by the writer by producing experimental anemias in animals and showing that the changes in the blood-making organs of intrauterine as well as of extrauterine life were similar in these animals to those observed in patients with pernicious anemia. Meyer (Münch. med. Woch., June 2, 1908).

SYMPTOMATOLOGY. — Pallor, the suggestive hallmark of all anemias, is usually well marked in the secondary type of this affection, and the subject's skin, mucosa, and nails may become so blanched as to appear almost colorless. In other instances, the loss of color is much more moderate, and in still others the actual pallor is more or less obscured by a yellowish or muddy or icteroid staining of the integument. In passing, it may be remarked that pallor of itself does not justify a diagnosis of anemia, for many persons with unnaturally pale faces have a perfectly normal blood-picture, in view of which the blood examination must invariably be the court of final appeal.

Pallor is often confounded with anemia. The blood should be examined in all cases of pallor, since many conditions may give rise to ochriasis, viz.: The emotion experienced by some patients when undergoing examination at the hands of the physician, their temporary pallor subsiding as they become more reassured; insufficient outdoor air and exercise, giving rise to insuffi-

cient peripheral circulation though the quantity and quality of the blood may be normal; ill-defined myxedema, in which the blood-vessels are narrowed by pressure upon them from the gelatiniform edema and sclerosis of the subcutaneous tissues. The resulting pallor may give rise to a faulty diagnosis of anemia. Though pallor may be due to the mechanical influences mentioned, thyroid insufficiency may, in itself, produce anemia; hence, the importance of blood examination; the scrofulous or lymphatic diathesis, with the thickening of the integument upon face and extremities, may produce pallor for the same mechanical reasons obtaining in myxedema, though examination may show the blood to be normal; aortic insufficiency with peripheral vasoconstriction gives rise to a pallor which at first sight suggests anemia; peripheral vasoconstriction is, in the majority of cases, responsible for the pallor seen in Bright's disease, though anemia secondary to the nephritis may occur. Finally, in a certain proportion of cases, a condition of oligohemia may be responsible for pallor, the quality of the blood being normal, though the quantity is insufficient to thoroughly irrigate the skin. M. Labbé (Gaz. méd. Nantes, April 11, 1903).

Aside from pallor, the most conspicuous symptom groups in anemia are attributable to disturbances of the cardiovascular, the gastrointestinal, and the nervous systems. Of the circulatory symptoms, dyspnea, cardiac palpitation, and dropsical swelling of the ankles and legs are likely to prove sources of great distress to the patient, while the discovery of hemic murmurs at the base of the heart and of a venous hum at the root of the neck affords findings of the utmost pertinence. These anemic murmurs, generally situated at or near the pulmonic orifice, are almost invariably systolic in time and restricted to the precordial area or to its immediate vicinity. They are sometimes associated with a perceptible increase in the size of the cardiac outline, indicative of dilatation of the heart from defective myocardial nutrition, overstrain, and, exceptionally, fatty degeneration.

Alterations in the size of the heart in anemic subjects. Dilatation is commonly met with, and sometimes, especially in chlorosis, elevation of the diaphragm displaces the heart upward and an apparent dilatation is found. Anemic dilatation is to be considered true idiopathic dilatation resulting from overstrain. None of the usual symptoms are present; gastralgia alone is complained of. Wybauw (Jour. méd. de Brux., Mar. 15, 1900).

There is nothing pathognomonic about the anemic murmurs which distinguishes them from the organic heart bruits. The most trustworthy characteristics of these murmurs are their slight tendency to transmission, their appearance during the systole, as a rule, over the area of the pulmonary artery, their variability and their increase in intensity in the standing posture and decrease in the recumbent position. As a rule, the general examination of the patient determines whether we have to deal with an anemic or an organic murmur. Orlofsky (Roussky Vratch, June 7, 1903).

The distinct positive venous pulse observed in endocarditis is not an uncommon symptom of anemia and is due to a relative muscular insufficiency of the tricuspid orifice. The cause is the same as that of the mitral insufficiency so common in chlorosis. In order to make sure of the functional character of the condition, it is important to bear in mind that a relative tricuspid insufficiency in anemia develops at the same time as the mitral insufficiency, while in endocarditis the tricuspid lesion usually develops long after the mitral. Besides, disturbances of compensation are usually absent. Von Leube (Zeit. f. klin. Med., Bd. lvii, Nu. 3-4, 1905).

The foregoing symptoms, which are prominent only in severe anemias, promptly vanish as the normal composition of the blood is regained, and frequently in such cases the pulse is inordinately rapid, of low tension, and subject to arhythmic disturbances, while occasionally the abrupt, jerky beat of the Corrigan pulse is superficially imitated.

Of the symptoms referable to the gastrointestinal tract, anorexia, pyrosis, abdominal distention, sensitiveness, and unrest, nausea, and constipation may attract attention. In the average case of secondary anemia the motor powers of the stomach are unaltered, and the secretion of hydrochloric acid remains normal or is even increased. On the other hand, there is a decided tendency toward weakening the intestinal motor function, although the juices of the gut flow naturally (Boas, v. Noorden).

Ulcers in the throat may be due to anemia or lowered vitality. The writer has seen 3 cases; all in young women. The ulcer is round, small, with scanty secretion. There was no history of either tuberculosis or syphilis and no swelling of the glands. Pohly (N. Y. Med. Jour., Aug. 27, 1910).

Of the various nervous disturbances, headache, vertigo, syncope, insomnia, phosphenes, muscæ volitantes, and tinnitus aurium are familiar examples. Moderate, irregular fever is occasionally observed as a consequence of nervous factors and as a sign of septic processes. Most anemics, particularly those of chronic character, complain of unnatural fatigue, both mental and muscular, and in severe cases the patient may be incapable of sustained intellectual effort, exhibits curious mental caprices and irritability, and develops a myasthenia amounting almost to complete debility.

Menorrhagia as a symptom of anemia must be regarded as a result of muscular inadequacy, the cause of so many varieties of uterine hemorrhage. The uterine muscle, by compressing the uterine blood-vessels, controls the blood-supply of the organ and the escape of blood from its lining membrane. Any defect in uterine wall muscularity, as compared with vascularity, permits of pathological uterine hemorrhage. For months before puberty the uterine muscle grows in bulk and the uterine vessels increase in size and number. When the first menstruation occurs, if the uterine muscle be well developed, as is usually the case, no undue hemorrhage appears, but if muscle growth lags behind vessel development muscular inadequacy permits prolonged and profuse bleeding. Puberty menorrhagia usually disappears in a few months, since muscle growth increases and gains control over the blood-vessels. W. E. Fothergill (Med. Chronicle, July, 1905).

Six cases of anemia of the central nervous system, resulting in sclerosis of the cord. The onset of the disease is gradual. The symptoms are very variable, as are the changes in the spinal cord. Sometimes the posterior columns are involved; sometimes the lateral tracts are added; again, there is a diffuse sclerosis of the entire cord. Paresthesia and ataxia may persist for years with few changes in the cord, or the intensity of the alterations may be much greater than the clinical symptoms. The mental state may be dull and inattentive, and there may be various muscular palsies of eye muscles or face. Leopold (Med. Rec., Mar. 5, 1910).

The blood-picture of secondary anemia is in no wise distinctive, as already pointed out in the remarks on the pathology of this affection. Usually there is a moderate and roughly parallel loss of hemoglobin and erythrocytes, the former being diminished approximately 45 per cent. and the latter 30 per cent. below the normal standard, in the case of

average severity. The stained film generally shows nothing more than simple pallor of the erythrocytes with, perhaps, a few misshapen cells and some tendency toward irregularity in their diameter measurements. Normoblasts and erythrocytes with stroma degeneration are met with only in anemias of great intensity, characterized by excessive destruction of the cells, and under such conditions an occasional megaloblast, indicating a fetal reversion of the marrow, may enter the blood-stream. Leucocytosis, developing under the circumstances referred to in a preceding paragraph, means stimulation of the marrow's functional activity, the exhibition of which is regulated largely by the nature of the exciting cause and by the individual peculiarities dominant in the case under consideration. The coagulation-time (*hematopexis*) of the blood is shortened in close relation with the degree of existing anemia.

Case of ankylostomiasis in which there were hemorrhages into the retina. The patients did not complain of their eyes, and yet hemorrhages were found in the retina. They probably constitute a constant symptom in severe forms of anemia due to ankylostoma. These hemorrhages appear in the form of round spots, bands, and semilunar marks (preretinal hemorrhages), and are chiefly found in the neighborhood of the posterior pole of the eye. Their presence has an unquestionable influence on the prognosis. They take place by diapedesis, are absorbent without leaving any traces, and do not give rise to any inflammatory symptoms. They occur chiefly in the layer of nerve-fibers, but may penetrate to the outer layers of the retina, even to the external limiting membrane. Changes in the smaller retinal vessels consist in swelling of the nuclei of the endothelial cells. Tchemolossoff (Roussky Vratch, Nov. 29, 1903).

It was at first believed that in severe anemia the relative and absolute consumption of O_2 and production of CO_2 diminished. Later it was shown (Kraus) that the gaseous metabolism tended, on the whole, to be increased above the normal rather than diminished in severe anemia, and was capable of still further increase on exertion. Patients with only 10 per cent. of the normal amount of hemoglobin are not rarely met with, and Nägeli has described one with only 7 per cent.; the authors set out to investigate how this drop in hemoglobin is compensated. In the first place, they remark that no other substance in the blood, besides the hemoglobin, can act as an oxygen carrier; further, in all anemias, except, perhaps, chlorosis, the total volume of the blood is lessened. Hüfner has always argued that the O_2-capacity of hemoglobin is constant, 1 gram of Hb taking up 1.34 c.c. O_2; but Bohr and many other writers bring forward good reasons for supposing that its specific O_2-capacity is variable—at any rate to the extent of 20 per cent.—and that hemoglobin is not a single or uniform chemical compound. Thus Kraus found that 1 gram Hb could take up from 0.9 to 1.97 c.c. O_2. Mohr found the specific O_2-capacity to rise from 1.26 to 2.0 c.c. O_2 per gram of Hb, in the course of six days and after two bleedings, and so was led to regard the variability of the O_2-capacity of the hemoglobin as a compensatory protective mechanism for use in anemia. Several observers have found the O_2-capacities (0.8 to 1.0 c.c. O_2 per gram of Hb) in patients with polycythemia rubra, and these observations have been used to explain the polycythemia noted in that condition. The authors believe that the O_2-capacity of blood varies with its coloration (=Hb-content) exactly, as Haldane stated, and they find this to be the case in polycythemia and in anemia. They were unable to find any increase in the O_2-capacity of the Hb in anemic patients; but in a number of these the percentage of oxygen used up in the capillaries was above the normal—venous blood is normally saturated with O_2 to the extent of about 60 to 75 per

cent., but in severe anemia perhaps only to the extent of 15 to 50 per cent. They agree with Mohr that this increase in the percentage of oxygen consumed in the tissues is an important compensatory mechanism in anemia. But it is not the only, nor indeed even the most important, compensatory mechanism; they believe that increased speed in the flow of blood through the vessels must be the most important of these. In two patients with polycythemia rubra they found no diminution in the maximum O_2-capacity of the hemoglobin, nor did the patients exhibit any increase in their tissue respiration such as Senator believed to obtain in this condition. Morawitz and Röhmer (Deut. Arch. f. klin. Med., Bd. xciv, S. 529, 1908; Med. Chronicle, Nov., 1909).

DIAGNOSIS.—The diagnosis of secondary anemia invariably must be based upon a suggestive blood picture plus the discovery of some factor responsible therefor. Given a blood poor in hemoglobin and erythrocytes in an individual suffering, for instance, with sepsis or gastric cancer or rheumatic fever, the diagnosis can tax no one's intelligence. But given an obscure etiological factor in an anemic person, one must carefully interrogate through a long list of potential causes of blood impoverishment in order to detect a satisfactory cause. The differential diagnosis of secondary anemia includes the consideration of pseudoanemia, chlorosis, pernicious anemia, splenic anemia, leukemia, chloroma, and Hodgkin's disease.

We must not judge entirely of the presence or absence of anemia by the volume and condition of the blood alone, but also by the function of the tissues which are dependent on the blood for their well-being. Thus 85 per cent. of hemoglobin, with 4,000,000 red corpuscles, may be normal for one individual in apparently perfect health, and yet another person of the same body-weight with this condition may suffer to a considerable degree from anemia. Brooks (Med. News, Oct. 21, 1905).

Pseudoanemia versus *true anemia* is a differentiation constantly to be borne in mind in examining a patient for the first time. Spurious anemia, which, of course, shows a normal blood report, is characterized by unnatural pallor of the skin and mucous surfaces, probably of hereditary origin and explainable on the grounds of a deficiency of skin pigment and abnormal constriction of the superficial capillary network. Apart from pallor, the affection is quite symptomless. In this connection may be mentioned an angiospastic type of pseudoanemia, recognized by the abrupt appearance of attacks of transient grayish pallor induced by emotion, fatigue, exposure to cold, and similar vasomotor stimuli.

Chlorosis, though its blood picture may be precisely counterfeited by certain forms of secondary anemia (such as *Chlorosis, q.v.*), is readily distinguished from the latter by its occurrence exclusively in girls and in young women who exhibit, with passable fidelity, a varied train of unmistakable chlorotic stigmata—greenish pallor, menstrual disturbances, perverted appetite, indigestion, constipation, slight enlargement of the thyroid gland, and many symptoms referable to functional neuroses.

Pernicious anemia in its typical form gives rise to three most pertinent blood changes: extreme oligocythemia combined with a disproportionately slighter oligochromemia; the presence of numerous erythroblasts, of which cells those of a megaloblastic type predominate; and many deformed and otherwise degenerate erythrocytes, notably megalocytes and basophilic corpuscles. The first

detail of this blood-picture means that the hemoglobin content of the erythrocytes (*color index*) is unnaturally high; the second indicates active compensatory hemogenesis and fetal reversion of the bone-marrow, and the last points to the manufacture by the marrow of numerous faultily formed, functionless erythrocytes, of little or no use as oxygen carriers. Leucopenia, relative lymphocytosis, and a moderate degree of myelocytosis are among the other hematological features of this disease. In addition to these findings, it must be recalled that true pernicious anemia arises insidiously, is entirely unconnected with any tangible causal factor, and invariably progresses steadily, perhaps with temporary periods of remission, to a fatal termination. An *aplastic type* of pernicious anemia has been described, in which, owing to extraordinary atrophy of the bone-marrow, there arises an intense oligocythemia and oligochromemia with but trifling evidence of structural degeneration and nucleation of the red corpuscles. In attempting the antemortem differentiation of aplastic anemia and anemia of the symptomatic variety (which attempt must needs frequently be conjectural), attention should be paid especially to these hematological peculiarities of the first-named disease: relatively low color index; absence of erythroblasts of both types—normoblasts and megaloblasts; scarcity of cells showing stroma defects and anomalies of shape and size, and extreme lymphocytic leucopenia. It is also helpful to remember that aplastic anemia is prone to affect young women, is commonly associated with severe hemorrhagic phenomena, and, arising from no apparent cause, pursues a fatal course of short duration, unbroken by periods of remission.

Splenic anemia, a rare and somewhat questionable clinical entity, causes a blood deterioration in no wise different from that accompanying an ordinary symptomatic anemia with leucopenia. But in splenic anemia there is an idiopathic splenomegaly without enlargement of the lymphatic glands, and, in the later stages of the disease, biliary hepatic cirrhosis, jaundice, and ascites supervene, to complete the symptom group sometimes spoken of as Banti's disease. Disturbances due to severe anemia and to the pressure of an enormous spleen are generally conspicuous, and the disease is likely to develop insidiously, drags along for several years from bad to worse, and eventually kills.

Leukemia is easily distinguished from secondary anemia by means of its distinctive blood picture, as well as by certain objective symptoms. In the myelogenous form the combination of a high leucocyte count and excessive numbers of myelocytes (*myelemia*) is conclusive, and in such cases the spleen is generally enormous; in the lymphatic variety the detection of a high absolute and relative lymphocytosis (*lymphemia*) is equally convincing, and here it is the rule to find great hyperplasia of the lymphatic glands.

Chloroma may account for an anemia identical with that of the secondary type, and it may also produce a blood picture closely comparable to that of lymphatic leukemia. In the former instance the low hemoglobin and erythrocyte values are accompanied by a relative increase in the number of lymphocytes, though the total leucocyte

count does not exceed normal, while in the latter the blood shows great anemia with decided lymphemia. This being the case, one must recognize chloroma not by any distinctive blood formula, but by the chloromatous symptom-complex, made up of exophthalmos, deafness, severe orbital pain, elastic swellings in the orbital and temporal regions, and the formation of metastatic "green tumors" in the periosteal structures.

In *Hodgkin's disease,* which in time gives rise to high-grade secondary anemia, the existence of a progressive glandular hyperplasia in the neck, axilla, and groin is conclusive evidence, apart from the presence of pressure symptoms, irregular fever, cutaneous bronzing, asthenia, and extraordinary emaciation, which together spell this malignant affection.

PROGNOSIS.—It is scarcely necessary to state that the prognosis in a given case of secondary anemia must depend upon the circumstances prevailing in the instance in question, the character, duration, and curability of the primary lesion being the decisive determining points of the forecast. The outlook in gastric cancer, for example, is very different from that in simple inanition or in one of the milder infectious diseases. On the whole, secondary anemia is a symptom that is promptly amenable to intelligent treatment, in strong contrast to which fact is the utter hopelessness of accomplishing a permanent cure in those deadly primary diseases of the blood, pernicious anemia and the leukemias.

TREATMENT.—Iron and **arsenic, nutritious food,** and **correct hygiene** will cure secondary anemia—provided that the essential cause of this symptom be removed. It is just as important to attend to a mass of bleeding piles or to treat an albuminuria in an anemic person as it is to prescribe hematinics, and, by the same token, it is equally important to outline a regimen in which an **out-of-door life, ample sleep,** and **rational personal hygiene** are items of strict observance.

The percentage of hemoglobin in infancy is below 55 at birth and not rising above 70 during the period properly so-called of infancy. The number of red corpuscles varies between 5,500,000 and 6,000,000. This low hemoglobin percentage is presumably due to an insufficient supply of iron in its food and the lack of sufficient reserve of iron in the liver at birth. It is probable that true chlorosis never occurs in infants as a disease, but it is a fact that the chlorotic type of blood is very common at this age. **Iron** is, therefore, specially indicated, but it is difficult to get infants to take iron by the mouth, and it is very liable, moreover, to disturb the digestion. It is desirable, therefore, to give it some other way, and infants take it subcutaneously without injury. A very serviceable form for subcutaneous use is the aqueous solution of the citrate. This can be put up in pearls, each one containing a single dose, in which form it remains sterile indefinitely. It is absolutely non-irritating, and never causes abscess or induration if properly given, though it is somewhat painful. A glass syringe with an asbestos packing, which can be sterilized, and platinum needle that will not corrode with the iron. The average dose during infancy is three-quarters of a grain every other day. He has used this treatment in a number of cases in different types of anemia and with pretty satisfactory results, even in the severe cases. In the mild cases the improvement was very rapid, and the writer's experience leads him to recommend the use of iron in this way. The results are more marked and more quickly obtained than by oral administration, and it is much less liable to disturb digestion. It is especially indicated in severe cases of secondary anemia

with digestive disorder and in those of a sclerotic type. J. L. Morse (Jour. Amer. Med. Assoc., July, 1910).

The form of iron to be administered, it is almost needless to state, should be readily absorbable, and unlikely either to upset digestion or to constipate. The **carbonate of iron,** in the pill suggested by Blaud, meets these requirements as well as any other preparation, and has the prestige of a long and dependable clinical usage. Excessive dosage is to be avoided, since the use of 6 or 8 grains a day will accomplish just as satisfactory results as a much larger amount, and will not tend to disturb the stomach or to constipate. **Ferratin** is a meritorious chalybeate, and is, if anything, even less astringent than Blaud's pill. Of the other iron preparations sometimes chosen for the same reason, the phosphate, lactate, and citrate all enjoy considerable vogue.

The most satisfactory result is obtained with the **peptomanganate of iron;** it is easily absorbed by the entire intestinal tract and evokes no concomitant effects. In 12 out of 23 cases the hemoglobin was normal after fourteen days; in 5 after three weeks, and in 5 after a month.

In acute anemia very good results were also obtained by this mode of treatment. H. Metall (Med. chir. Centralbl., June, 1902).

Inorganic preparations of iron are well utilized by the organism and give better and more rapid results than organic preparations, the most rapid and marked increase in hemoglobin being seen after endovenous injection of inorganic preparations of iron. Experimentally there was but slight difference seen in the effects of inorganic and organic preparations administered through the digestive tract, the results obtained depending, in both classes, upon the amount of iron contained in them. F. Aporti and S. Aporti (Il Policlinico, Sept.-Oct., 1902).

Subcutaneous injections of the **arsenate of iron** valuable in anemia. In a previous article the author has shown that injection of iron salts, if continued for a sufficient length of time, produce very constant and trustworthy results in anemia. The arsenate of iron used because the addition of arsenic improves the action of iron. This method of treatment used in a large number of cases and considered the best mode for administering iron. The author employed the solutions prepared by Zambeletti, in which the arsenate was perfectly dissolved. The injections were made preferably into the nates, with the usual aseptic precautions, by means of a syringe with a rather long needle. The doses were gradually increased until about 60 or 80 injections had been given, when the doses were gradually diminished again. Toward the end of the treatment the injections were alternated with the administration of **iron, arsenic,** and **phosphorus,** as well as **nux vomica** or **strychnine** by mouth, the latter being continued for some time after the injections were abandoned. The results obtained with this method of treatment were uniformly satisfactory in a large number of cases. Nicola Fedele (Gaz. degli osped. e delle clin., Feb. 1, 1903).

The headache of anemia is due chiefly to the deficiency of hemoglobin, and consequent tendency to edema, with the simultaneous starving of the meninges. It is usually frontal, but may be vertical. In certain individuals of lymphatic type, subject to anemia, chilblains, and cold extremities, there may be a deficiency of calcium salts in the blood, and the administration of the calcium salts may be of great service in relieving the headaches of such patients. The lactate should be given in doses of 15 to 20 grains, three times a day. The headaches of the morning after copious libations have been ascribed to a lack of calcium salts in the blood, these having been precipitated by the organic acids contained in the wine.

This headache may be very quickly removed by a dose of 20 to 30 grains of calcium lactate shaken up with a

little water. Wilfrid Harris (Practitioner, July, 1906).

There has been distinct progress in the treatment of anemia. The first of these is the method of **direct transfusion** introduced by Crile, whose experiments and results the author considers a brilliant illustration of the value of vivisection to humanity. The second is the use of **colonic irrigations** in pernicious anemia, as recommended by Herter, and successfully employed by Ditmar and Hollis. Herter's discovery that special putrefactive processes in the intestines are due to the prevalence of anaërobic bacteria, particularly the *Bacillus capsulatus aërogenes,* and the parallelism of their presence with the symptoms of the disease suggested this treatment by injections, which the writer considers a valuable therapeutic advance. The third point touched on in his paper is the establishment of the clinical value of **inorganic iron** in the treatment of anemia. Ingested iron, like the carbohydrates, is converted into intermediate organic compounds and enters into the reserve iron stored up in the body, which is normally in excess of the needs of the system. S. J. Meltzer (Jour. Amer. Med. Assoc., Aug. 24, 1907).

Employing the hemoglobin contents as an index of the degree of secondary anemia, as well as an actual erythrocyte count, the writers found that the hypodermic use of the **citrate of iron** in the secondary anemia of tuberculosis permitted them to control the anemia with almost mathematical precision, and that it actually in no single instance failed to improve the quality of the blood to at least some degree in the 256 cases in which they had employed it. Over 70 per cent. of these cases were in the advanced and far advanced classes, in which the anemia is a commonly manifested phenomenon. The measure was uniformly successful in raising the hemoglobin standard to normal in all cases in which the patient might be considered to be doing well, or in which the status quo was seemingly maintained.

It is not necessary to use a larger dose of citrate of iron than 0.05 Gm. Others who have used larger doses have observed sudden vomiting to follow its administration. The technique of the method is to employ the ordinary hypodermic syringe and needle, selecting the buttock as the least inconvenient site of injection, and giving an injection daily until the result is obtained. E. S. Bullock and L. S. Peters (Jour. Amer. Med. Assoc., Oct. 28, 1911).

Arsenic is of indispensable value as an adjunct to iron in dealing with anemia, particularly those forms distinguished by relatively excessive oligocythemia, as in those severe instances consequent to infectious and malignant processes. The time-honored **Fowler's solution** answers well in the majority of cases, but where an idiosyncrasy exists toward this preparation, as it frequently does, or where it is imperative to stimulate hemogenesis very rapidly, **atoxyl** (sodium anilarsenate) will prove the better form of arsenic. It should always be given hypodermically, in doses of from ½ grain to 2 grains, on alternate days, until the patient has received about 20 grains, after which the drug is discontinued for a week, and then readministered according to the plan originally followed. Given in this manner, one need not fear that lamentable complication, optic neuritis, which has been produced by the ill-advised use of atoxyl. Or **arsacetin** (sodium acetyl arsanilate) may be used, in the same dose and by the same method advised for atoxyl, if it is thought best to employ an even less toxic preparation of arsenic. While useful, manganese, phosphorus, red bone-marrow, hemoglobin, oxygen, and the cacodylates are in no sense adequate substitutes for iron and arsenic in the treatment of anemic conditions.

Hypodermic medication with **iron** and **arsenic**, together with **strychnine** and the **hypophosphites**, offers a prompt and powerful reconstructive adjunct to the pure air, good food, and sensible hygiene that are essentials in pretuberculous conditions. The **green ammoniated iron citrate** can be introduced into the system, without danger, in doses of from ¾ to 1½ grains, while **sodium arsenate** is given in doses of from 1/60 to 1/30 grain. The injections of solutions of these drugs are given deeply into the muscles of the buttocks or back. Only slight pain attends the procedure, and a general feeling of well-being follows the treatment. A full dose of the iron within five minutes causes a feeling of tension in the head, tingling sensations, and a flushing of the face. Doses larger than 1½ grains may cause nausea or vomiting. B. R. Shurly (Jour. Amer. Med. Assoc., June 16, 1907).

The anemic subject should eat plentifully of **nutritious, and,** it must be insisted, **palatable, food**—red meats, strong broths, eggs, butter, cream, fruits, and ferruginous vegetables like spinach, asparagus, lentils, and cauliflower. If the appetite flags it may be advisable to whip it up with a glass of **stout** or of **mild claret** at mealtime, or by the use of the **bitter tonics**, the amount of food at the same time being intelligently restricted. Indigestion, if not forestalled by a rational dietary, must be combated by such useful remedies as **pepsin** and **hydrochloric acid, pancreatin** and **diastase, pawpaw, charcoal,** and **bismuth.** It is most necessary for the patient to have a free bowel movement each day, to insure which, if other measures fail, it is good practice to resort to **cascara sagrada, phenolphthalein,** singly or combined with **aloin, strychnine,** and **belladonna,** and supplemented by a dram or two of **Carlsbad salts** dissolved in a tumblerful of hot water, to be slowly sipped each morning directly on arising. Intestinal fermentation, the bane of so many anemics, is best treated dietetically (eggs are notorious offenders), by **intestinal irrigation,** by the administration of cultures of the **lactic acid bacillus,** and by the use of **B-naphthol, salol, bismuth salicylate, phenol,** and similar antifermentative drugs. In patients with troublesome nervous symptoms **strontium bromide** and the **valerianates of iron, quinine,** and **zinc** are helpful adjuncts to the therapeusis suggested above.

Alimentary fermentation being in great measure responsible for the blood deterioration of anemic states, **lysol** is a good intestinal antiseptic to correct this condition. Under its influence the movements from the bowels become fewer, formed, less foul, and free from mucus; the appetite becomes increased, and the patients rapidly gain strength. The drug is given in capsules containing each 1½ minims; one capsule every two hours. F. Burges (Münch. med. Woch., Nu. 9, S. 416, 1905).

Case of probable hemophilia in a child of 2 years. The anemia from the repeated losses of blood was combated by **injection of** from 10 to 18 c.c. of **defibrinated blood** from healthy adults. The improvement under these injections was pronounced and striking, and the restoration of normal conditions in the blood was accompanied by improvement in the general health. Five of these injections were made in the course of six weeks. It is useless to attempt this transfusion of blood, according to the writer, when the blood-producing apparatus is irreparably injured. It should not be done as a last resort, but should be tried as early as possible when anemia in children is assuming a grave form. The injections were made under the skin of the thigh. Some substance in the serum evidently acts as a stimulus for the blood-producing organs.

Schelble (Jahrb. f. Kinderheilk., Oct., 1908).

In anemia due to autointoxication from the gastrointestinal tract, as often occurs in chlorosis: 1. Favor gastric functions by **proper diet.** 2. Secure regular bowel movements by **laxatives.** 3. Begin the use of iron, giving following pill: **Subcarbonate of iron,** 0.10 gram (1½ grains); **powdered aloes,** 0.02 gram (⅓ grain); **extract of rhubarb,** 0.05 gram (¾ grain); two pills before meals. Huchard and Fiessinger (Revue de thérap., March 15, 1910).

The gastric and hyper- esthesia in anemia and chlorosis were favorably influenced in several instances by aluminum silicate, given in the form of **neutralon,** in doses of ½ to 1 dram in 3 ounces of water, one-half to one hour before meals. Rosenheim and Ehrmann (Deut. med. Woch., Jan. 20, 1910).

In the management of acute anemias of grave character (*i.e.,* post-hemorrhagic variety) the **direct transfusion of an homologous blood,** by Crile's or by Carrel's method, may prove to be a life-saving expedient. The technique and other details of this operation are discussed elsewhere in this work. (See TRANSFUSION.)

Seven cases of severe anemia greatly benefited by **transfusion** of only 5 c.c. (75 minims) **of human blood.** No benefit was observed in cases of leukemia. Transfusion of this amount is generally harmless, though the blood from certain persons showed some toxicity. Weber (Deut. Archiv f. klin. Med., Sept. 4, 1909).

Four cases of severe anemia greatly benefited by **intramuscular injections of defibrinated blood.** The writer drew off venous blood from a healthy subject into a small flask, stirred for ten or fifteen minutes, filtered through wool, and incubated for one-half to one hour. He then injected 10 to 30 c.c. in the gluteal muscles; the procedure is almost painless. Arsenic in increasing doses should be given at the same time. Huber (Deut. med. Woch., June 9, 1910).

Observations on twenty dogs killed by chloroform and resuscitated after periods varying from three to fourteen minutes, with a view to determining the limits of recovery after a total anemia of the nervous system. In human resuscitation the technique is as follows: The patient, in the prone posture, is subjected at once to **rapid rhythmic pressure on the chest,** with one hand on each side of the sternum. This pressure produces artificial respiration and a moderate artificial circulation. A cannula is inserted, toward the heart, into an artery. **Normal saline,** Ringer's, or Locke's **solution,** or, in their absence, sterile water, or, in extremity, even tap water is infused by means of a funnel and rubber tubing. But as soon as the flow has begun, the rubber tubing near the cannula is pierced with the needle of a hypodermic syringe loaded with 1 : 1000 **adrenalin chloride,** and from 15 to 30 minims is at once injected. The injection is repeated in a minute if needed. Synchronously with the injection of the adrenalin the rhythmic pressure on the thorax is brought to a maximum. The resulting artificial circulation distributes the adrenalin, that spreads its stimulating contact with the arteries, bringing a wave of powerful contractions and producing a rising arterial, hence coronary, pressure. When the coronary pressure rises to, say, 40 mm. or more, the heart is likely to spring into action. Just as soon as the heart-beat is established the cannula should be withdrawn. Bandaging the extremities and abdomen tightly over the masses of cotton is very useful. From a personal experience in attempts at resuscitation of the human being it became apparent that the human heart seems to respond even more readily than the heart of a dog. Crile (Amer. Jour. Med. Sci., Apr., 1909; Jour. Amer. Med. Assoc., May 1, 1909).

Hydrotherapy and **general massage** must be regarded as most useful aids to the drug treatment of anemia, and such measures, when sanely car-

ried out, will do much to promote adequate excretion and secretion, to maintain a healthy balance of the blood and lymph streams, and to stimulate oxygen and carbon dioxide interchange. A regimen of **fresh air, sunshine,** and **gentle exercise** is of great value, added to the foregoing hygienic measures, and in this connection it is interesting to recall Gardinhhi's statement, recently voiced by Pope (N. Y. Med. Jour., November 2, 1907), that the presence of sunlight promotes the absorption of iron from the liver, where this metal, after ingestion, is presumably stored in no inconsiderable quantity.

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ANEMIA, SPLENIC. See Spleen, Diseases of.

ANESIN. See Chloretone.

ANESTHESIA. See Various Anesthetics: Ether, Chloroform, etc.

ANESTHESIN. — Anesthesin is, chemically, ethyl para-aminobenzoate [$C_6H_4.NH_2.COOC_2H_5$]. It occurs as a white, odorless, and tasteless powder, almost insoluble in cold water, with difficulty soluble in hot water, sparingly soluble in fatty oils (2 to 3 per cent.) and in dilute glycerin, easily soluble in alcohol, ether, chloroform, benzene, and acetone. It melts at 90° to 91° C. Though decomposed by prolonged boiling, it can be rendered sterile without deterioration when dissolved in oils. Alkalies and alkaline carbonates are incompatible with it, removing the ethyl group to form alcohol and setting free para-aminobenzoic acid.

PHYSIOLOGICAL ACTION. — The most conspicuous feature of anesthesin is its local anesthetic property. The drug differs radically from cocaine in that it is but very feebly toxic and is insoluble in water. The low toxic power was shown in the experiments of Binz, who administered 0.6 Gm. (10 grains) of the drug in 20 c.c. of oil by stomach tube; on the next day the animal was in good health, with urine normal. The dose required to kill was found to be 1.15 Gm. (18 grains) per kilo of animal, the symptoms produced being paralysis, gradual loss of sensibility in the hind limbs, and dyspnea terminating in asphyxia. The drug was also administered intravenously in dogs and intraperitoneally in guinea-pigs, with similar results indicative of a low degree of toxicity.

The intoxication produced by anesthesin is in some ways comparable to that of acetphenetidin; massive doses lead to the formation of methemoglobin, with consequent methemoglobinuria.

Anesthesin placed upon the tongue produces a feeling of numbness in two to three minutes. By virtue of the insolubility of this substance, its anesthetic action is more strictly localized than that of cocaine. It is also feebler, but is more enduring. It is said to exert no action on the vessels at the site of application, causing neither vasoconstriction nor vasodilation. Over orthoform it has the advantages of being more stable and practically non-irritating.

THERAPEUTIC USES. — Internally, anesthesin, as first demonstrated by von Noorden, is useful in conditions of **gastric hyperesthesia,** including **nervous dyspepsia** and **gastric ulcer.** The dose is 0.2 to 0.5 Gm. (3 to 7½ grains) ten to fifteen minutes after the ingestion of food. In **laryngeal tuberculosis** an insufflation of anesthesin has been found by Courtade to arrest the severe pain and, therefore, the dysphagia for nearly forty-eight hours. Earp found it very useful in very painful bleeding external **hemorrhoids.** The bowels were moved freely by enemas, hot applications were used freely, and the following ointment was applied twice daily:—

℞ *Anesthesin*	.....	15 grs. (1 Gm.).
Ergotin	.....	1 dr. (4 Gm.).
Ichthyol	.....	30 mins. (2 Gm.).
Lanolin	.....	3 drs. (12 Gm.).
Petroleum	..to make	1 oz. (31 Gm.).

Earp also found anesthesin useful in perineal **eczema** which had not yielded to other measures. S.

ANEURISM. —DEFINITION.— An abnormal circumscribed blood-tumor containing a cavity communicating with an artery. An aneurism consists of a sac, neck, and contents. The contents include liquid blood, coagula, and laminated fibrin. Aneurisms vary in size from that of a millet seed to that of a child's head. In order of frequency aneurisms involve the thoracic aorta, popliteal artery, femoral artery, abdominal aorta, subclavian artery, innominate artery, axillary artery, iliac artery, and the cerebral and pulmonary arteries.

VARIETIES.—**Congenital.** — Congenital aneurisms are extremely rare, but they have been reported involving the abdominal aorta and ductus Botalli. A rare congenital deficiency of the elastic elements of the walls of the arteries may be the cause of multiple aneurisms, especially involving the smaller arteries of the body.

Idiopathic. — Idiopathic aneurisms are those arising without obvious traumatic injury to the vessel wall. They are usually dependent upon disease of the artery, and constitute most of the aneurisms involving the great vessels of the trunk, and the smaller aneurisms of the brain and other viscera.

Traumatic.—Traumatic aneurisms are those resulting from mechanical injuries sustained by the arterial wall, either in the form of a contusion, incision, or laceration.

Hernial.—Hernial aneurisms are usually small traumatic aneurisms produced by the bulging of the inner tunic through the divided outer layers of the arterial wall.

True.—True aneurisms are those having walls formed by the normal coats of an artery. It is rare, however, to find an aneurismal sac in which intima, media, and adventitia can all be demonstrated.

False.—False aneurisms are those in which the sac is formed by tissues other than those derived from the wall of the artery. They follow arterial incisions or ruptures, but even with these false sacs the endothelium proliferates from the intima of the artery into the sac and finally tends to line it.

Diffuse.—Diffuse aneurisms are false aneurisms resulting from an extensive extravasation of blood from an open artery. As a rule, they are due to traumatism, but they also result from the spontaneous rupture of a diseased artery.

Dissecting. — Dissecting aneurisms are those in which the aneurismal sac lies between the coats of the artery. As a rule, they have two mouths, the blood entering through one opening, separating the layers of the arterial walls, and then, at some distance, recommunicating by a second opening with the arterial stream. These occur most frequently in the abdominal aorta and may produce a very extensive separation of the arterial coats.

Embolic.—Embolic aneurisms are those resulting from the lodgment of emboli. By some they are attributed to the laceration of the walls of the small vessels by calcareous embolic particles. It is evident that they may also result from degenerative or inflammatory changes of the arterial wall, secondary to the lodgment of the embolus.

Embolomycotic aneurisms develop during the course of endocarditis and occasionally during some of the acute infectious diseases, which form a distinct group by themselves, differing in pathogenesis, clinical course, and prognosis from those developing secondary

to chronic arterial changes. They have been recognized since 1851. They may develop in one of three ways. Most commonly they follow an endarteritis associated with lodgment of infected emboli at the bifurcation of arteries. A few cases have been reported which developed during the course of infectious diseases unaccompanied by endocardial changes. The possibility of traumatic origin is also supported by the observation of Ponfick and Thoma of calcified emboli in the arterial wall and projecting into the aneurism. Clinically, embolomycotic aneurisms differ from those following chronic arterial changes: (1) in developing at an earlier age; (2) in frequently being multiple, acute and chronic forms often occurring in the same individual; (3) in the frequent involvement of visceral arteries, and (4) in the tendency to remain small. A number of cases have been reported in which no satisfactory explanation is given of the cause. About one-fourth of the cases observed developed during the third decade of life, and about one-fourth during the second.

They are much more frequent in males, although the authors have been unable to demonstrate the reasons for this satisfactorily. They have collected, including their own cases, 96 aneurisms of this class occurring in 65 patients, they frequently being multiple, and report 3 cases observed by themselves. The largest proportion of these aneurisms occurred in the superior mesenteric and cerebral arteries, and in the aorta, which is in marked contrast to the distribution of the ordinary type of chronic aneurisms, which rarely occur in the superior mesenteric or cerebral arteries. There is nothing characteristic in the symptoms, and they are not often suspected until fatal abdominal or cerebral hemorrhage occurs. Bacteria have been found within the wall of the aneurism, showing the bacteriological relationship between the vegetations on the heart valves and the clot in the aneurism. The forms are usually the streptococcus and staphylococcus, though other species have been reported. In 2 of the author's cases, examinations revealed the pneumococcus. This infection of the aneurisms complicates any operation, the patients being usually in a critical condition and not enduring surgery well. Dean Lewis and V. L. Schrager (Jour. Amer. Med. Assoc., Nov. 27, 1909).

Miliary. — Miliary aneurisms are very minute aneurisms most frequently observed in the brain or lungs. They involve small- or medium- sized arteries and often occur in great numbers.

Fusiform or Ectatic. — In these forms the weakened arterial walls yield in every direction, forming a fusiform, or, rarely, a somewhat cylindrical, enlargement. The three coats of the artery may be demonstrated in the sac; usually there is little clot present, and there may be few symptoms, unless through weakness of a part of the wall a sacculated aneurism follows. The walls of the fusiform aneurism may be thicker than that of the adjacent artery.

Sacculated.—Sacculated aneurisms are due to the bulging of one side of an artery. The elastic and muscular layers of the artery are not found in the walls of the sac.

ETIOLOGY. — Aneurisms result from conditions weakening the arterial wall and increasing the blood-pressure.

Race. — The Anglo-Saxon race is most frequently affected; the English more than the American, a condition attributed to the greater consumption of alcohol in England. Aneurism is rare in the Asiatic races and in Italy. It is three times as prevalent in the American negro as in the white race.

Age.—Aneurism is most frequent between the ages of 30 and 50, a period when degenerative changes in the ar-

teries are especially found in those engaged in laborious physical work.

Sex.—Men are affected ten times as frequently as women, excepting the carotid and dissecting forms of aneurism, which occur more frequently in women. The more laborious occupations of men and their greater tendency to dissipation and excess explain the influence of sex.

Soldiers, sailors, athletes, cab drivers, furnace men, and others engaged in violent, but intermittent exercise are especially predisposed to aneurism. It is eleven times more frequent in the English army than in the civilian, and is much more frequent in soldiers than in sailors, a condition attributed to the pressure and strain from poorly fitting clothing and heavy accoutrements. Cab drivers, apparently from the pull upon the arms, are especially susceptible to thoracic aneurism.

Vessels at the point of flexion and extension, such as the popliteal and iliacs, or under greater strain, such as those of the right arm rather than the left, are more frequently involved. Occasionally symmetrical aneurisms, as double popliteal aneurisms, occur.

Those conditions that produce a weakening of the arterial wall, especially all the causes of arteriosclerosis and atheroma, are important predisposing causes to aneurism. These include syphilis, alcoholism, rheumatism, gout, and the action of mineral poisons like lead.

> Arterial disease appears to be rare, almost unknown, in animals. Syphilis, being probably peculiar to man, is by this observation placed more firmly in the list of etiological factors. Arterial disease in children under 6 years, even in those who are victims of congenital syphilis, is practically unknown. In those from 6 to 15 years it is rare. It is found in the initial stage most commonly between the ages of 30 and 40 years. The teratological factor, though an undeterminable one, is of great importance. Arterial disease seems to be attributable to syphilis in about 32 per cent., to tuberculosis in about 16 per cent. The facts presented go to show that the colored race is affected about four times more frequently than the white.
>
> General arteriosclerosis seems to be not commonly found with aneurism, and its presence may be considered as evidence against the probable development of aneurism.
>
> Staining with selective stains and treating with a chemical which digests tissue show the elastic tissue to be free of histological alterations, suggesting that this tissue undergoes physical or molecular rather than histological change. C. N. B. Camac (Amer. Jour. Med. Sci., May, 1905).

The influence of rheumatism is one of great importance, especially in young patients. The writer, working with Rénon, has recently published some important observations relative to this subject. According to the cases collected by this author, the average age is from 10 to 16 when the patients have usually had several attacks of acute rheumatism. Repetition of the disease is regarded as an essential factor. The appearance of aneurism is preceded for some time by the signs of aortic incompetence and hypertrophy of the heart. After a period of considerable latency, the symptoms and signs of aneurism appear rapidly. They are dyspnea, especially marked after effort, and characterized by forced inspiration without actual oppression. After a short time this dyspnea becomes permanent, though occasionally varied by pseudoasthmatic crises, sometimes attacks of pain resembling angina pectoris. The attacks usually appear during the first sleep. The patient retires to rest in his ordinary condition, but suddenly awakes in great agony, complaining of a feeling of constriction in front of the chest, air hunger, desire to cry out, and violent inspiratory efforts are made. The crisis may last

from a quarter to one hour, and then gradually disappear. Occasionally the crises are entirely painful without respiratory trouble. They may, therefore, be pseudoasthmatic or pseudoanginal. Considerable intervals may elapse between them, for in one case quoted by the author they numbered 2 or 3 during the year; in others they are more frequent, occurring once a month, or even daily. The diagnosis is confirmed by the rapid appearance of physical signs. These aneurisms, as a rule, affect the upper right costal area, and do not differ from those usually observed in other cases. Aortic aneurism in young rheumatic subjects may develop fully in the course of a few weeks, sometimes in succeeding stages corresponding to the rheumatic crisis. After each crisis there may be temporary improvement, due to retrocession of the tumor. This improvement is reversed by a fresh crisis of articular inflammation. The condition is, therefore, progressive, and there is little hope of obliteration taking place in the sac. Prognosis is usually fatal, death often occurring suddenly either from hemorrhage or as the result of an anginal seizure.

Treatment can only be directed toward symptoms, nitrites being given for dyspnea and pain, and salicylates should not be omitted in view of the rheumatic nature of the disease. Feytaud (Thèse de Paris, 1906; Brit. Med. Jour., Jan. 12, 1907).

Generalized arteriosclerosis or endarteritis is seldom followed by aneurism of any of the large blood-vessels, the pathogenic conditions of which are forms of progressive periarteritis, finally causing perforation of the elastic membrane of the affected vessel. Aneurisms of this kind—those due to traumatism being excluded—have an infective origin, and are the result of tuberculosis, syphilis, or malaria. Lancereaux (Rev. de chir., No. 8, 1906).

Aneurism of the thoracic aorta is undoubtedly a syphilitic disease, though aortic strain from hard work where the tissues are already degenerated by alcoholic excesses must certainly predispose. A strong alcoholic history was obtained in more than 40 per cent. of the writer's cases. Of 225 cases of aneurism, 179 were sacculated, 39 fusiform, and 7 dissecting. In much the larger proportion of cases the aneurism occurs in the transverse portion of the arch of the aorta. Drummond (Brit. Med. Jour., June 13, 1908).

Cardiac hypertrophy, plethora, and renal disease are also factors. Experimentally, aneurism may be produced by the repeated introduction of adrenalin into the circulating stream.

PATHOLOGY.—Idiopathic aneurisms develop in an area of atheroma, in the situation of an old scar, the point of lodgment of an embolus, or other weak area in the arterial wall. All forms of aneurism are lined by endothelium, excepting the fusiform aneurisms; the media of the artery does not constitute a layer of the abnormal sac. This is important, and it means not only that the normal muscular and elastic coats are absent, but that the vasa vasorum upon which the arterial wall depends for its nourishment is lacking. The sacs of all saccular aneurisms tend, therefore, to be weak and from the blood-pressure to become progressively distended.

In the fusiform aneurism all the layers of the arterial walls may remain and the wall of the sac may be thicker than that of the normal artery, the intima being thickened by atheroma, the adventitia by the deposit of fibrous tissue, while the middle coat is thinned. As the inner coats of an artery constitute not less than three-fourths of the thickness of its wall, containing the elastic and muscular layers, and also the vasorum supplying the walls with nourishment, the thinning, absence, or damage to these structures means a weak and poorly resilient wall for the aneurismal sac.

In sacculated aneurisms there is usually a progressive deposit of layers of fibrin against the wall of the sac, tending to strengthen the walls and to lessen the fluid contents. The lessening of the fluid contents is important, as the pressure on the sac wall varies as the square of the diameter of the cavity which contains the fluid.

At times the blood-clot is deposited in progressive layers until the entire sac is filled, resulting in a spontaneous cure. The blood-clot at the periphery is white, laminated, and fibrous, although rarely organized into the true fibrous tissue, the lack of vasorum preventing vascularization. The aneurism, therefore, may consist of a sac or body, which in the sacculated form may communicate by neck and opening with the artery. The sac is strengthened on the outer side by the deposit of fibrous tissue, an evidence of the reaction and irritation of the tissues against which the aneurism presses.

The sac may contain peripherally white, laminated clot; then a layer of softer, red blood-clot, and finally fluid blood communicating with the blood-stream. In the cylindrical and fusiform aneurisms little or no lining clot may be present.

The size and shape of the sac are modified by adjacent pressure. Rotation of the sac may occur so that in a fusiform aneurismal sac the orifices of the efferent and afferent trunks may lie at the sides or at the equator of the sac, rather than at the poles.

Matas classifies aneurisms by the number of orifices which connect them with the parent artery. These orifices may only be accurately determined after the opening of the sac. Fusiform aneurisms have two distinct orifices; saccular or sacciform aneurisms are those which are connected with the lumen of the parent vessel by a single circular, ovoid, or elongated opening through which the blood flows in and out the sac.

The sac of the aneurism may have many collateral branches corresponding somewhat with the branches normally given off by the segment of the arterial wall forming the aneurism. These collaterals may be functional or impervious and containing thrombi. The perianeurismal circulation may be very important in maintaining the collateral circulation after operation upon the sac. An aneurism influences the blood-stream, absorbing the cardiac wave, so that the pulse distal to the sac is delayed and weakened. To compensate for this the heart may hypertrophy and anastomotic channels form.

The aneurism may so press upon the main vessels as to completely interrupt the circulation beyond the sac. The adjacent tissues are variously affected. Bone is eroded and progressively destroyed by the continuous pressure, cartilage being much more resistant than bone.

Nerves are stretched, compressed, and flattened, at times destroyed, giving rise to paresthesia and more rarely paralysis. Adjacent veins may be compressed with the production of cyanosis and edema, and rarely erosion and perforation in the venous channel occur. Mucous canals are compressed and displaced, while fibrous tissue, tendons, and fascia are flattened, stretched, and often incorporated into the sac.

Thrombi may form in tributary vessels, and emboli may result from the dislodgment of clot or fibrin. Cerebral complications, such as hemiplegia, infarcts in the internal organs, and gangrene of the extremities, also occur.

SYMPTOMS.—Aneurismal dilatation may occur suddenly from traumatism or a great increase of intravascular pressure and may be characterized by sharp pain and rapid enlargement along the course of an artery. The sac, however, usually forms slowly and at first without pain or any other symptom.

> Case of a woman aged 42 years, attended by remarkable features. The aneurism was eroded and perforated the sternum in two places without ever causing pain or any other pressure symptoms; it presented externally as a tumor, and then disappeared under treatment by iodide of potassium, the skin rupturing without letting out any blood. This series of events was repeated several times in the course of seven years. Death occurred from the sudden bursting of the aneurism as the patient lifted a pitcher of water. R. C. Cabot (Amer. Jour. Med. Sci., April, 1900).

The diagnosis of aortic aneurism still remains in obscure cases a difficult one, and even the X-ray examination may be misleading. Attention called to the frequency with which, in aneurism of the arch, the left supraclavicular groove is obliterated or even bulges, and the left external jugular is obviously fuller than the right. The anatomical reason lies simply in the compression of the left innominate vein as a result of the dilated arch. A mediastinal tumor may have the same effect, but dilatation in cases of aortic insufficiency is apparently seldom sufficient to effect compression. Dorendorff (Deut. med. Woch., Nov. 31, 1902).

Pain is one of the earliest and most constant symptoms of aortic aneurism. It was the first and most severe symptoms in about half of the author's cases. It is possible that it should be absent, though there may be dyspnea, cough, and cyanosis, and though the sac may perforate the chest wall or erode the spine. The most common situation for the pain is in the region of the heart itself, radiating to the neck, the shoulder, and back, and down the left arm or both arms. In some cases the abdominal pain is severe. Several distinct varieties of pain may be recognized in this disease: 1. Attacks of true angina, having paroxysms of pain of maximum intensity, with radiation to the arm. 2. Sharp neuralgic pain due to pressure on the nerves, perhaps extending along the course of the nerves, and associated with herpes when the descending thoracic aorta is implicated. It is similar in character to that which is caused by the pressure of pelvic tumors, and by disease of the vertebræ, and it may be paroxysmal in character. 3. Pain of a dull, boring character which is present when the chest wall or the spine is eroded by the aneurismal sac. This is the form of aneurismal pain which is most enduring and most severe. It is due to tension and stretching of fibrous and bony structures rather than to pressure upon nerve cords. 4. Pain referred to the nerves of the arms or the skin in the precordial region or to the pectoral or sternomastoid muscles.

One object of the writer's paper was to narrate types of cases in which attacks of angina pectoris customarily precede the appearance of the aneurism for months or years. The paroxysms may not be in the least suggestive of aneurism, but they are associated with early structural changes in the wall of the aorta. In sclerosis of the aorta pain is not necessarily a symptom, the author having observed this fact in syphilitic patients. With lesions of arteries the pain may be the most intense, this being frequently observed in embolism, thrombosis, and the ligation of vessels. W. Osler (Med. Chronicle, May, 1906).

With the exception of the rare cases in which there is trouble with swallowing, the early symptoms of aneurism, manifested by pressure, are usually either pain or disturbance with the respiratory apparatus. The latter may come either from pressure on the air passages or from pressure on the recurrent laryngeal nerve. The symptoms frequently simulate those of heart

disease, and their true meaning is learned partly by not finding a cardiac condition that will explain the symptoms, and partly by looking for and finding evidence of an aneurism.

The picture of aortic aneurism in its earlier stages is not uniform, but varies widely with the position and size of the aneurism. There are no pathognomonic signs. The most characteristic feature of one case may be entirely lacking in the next one. And yet a careful physical examination and a careful consideration of the physical signs and symptoms should enable the detection of the existence of an aneurism of the ascending or transverse arch at a very early stage. The X-ray examination is of use in the case of aneurisms in these two parts of the aorta as confirmatory evidence, as giving more definite information in some respects, and sometimes (when pulsation is seen) in deciding between an aneurism and a solid tumor. The X-rays may detect aneurisms of the descending arch and the descending thoracic aorta which cannot be detected by the ordinary methods of physical examination. On the other hand, a negative report of an X-ray examination is not absolutely conclusive proof against the existence of an aneurism.

The detection of an aneurism of the arch of the aorta requires no greater skill than does the recognition of incipient tuberculosis. It is, therefore, within reach of the general practitioner, if he will give this disease equal consideration with tuberculosis. When discovered early, the treatment is not the same as in the advanced stages. Moderate limitation of exertion and mental quietude are essential, but absolute rest in bed is not necessary. While the disease cannot usually be cured, life can be prolonged in comfort. The vasodilators are the most useful drugs so far as medication is demanded. H. D. Arnold (Amer. Jour. Med. Sci., April, 1908).

An early postive diagnosis of aortic aneurism is obtainable only by the X-ray. Expansile pulsation is not constant. Abnormal dullness is a valuable sign when present. The most constant sign is systolic bruit, which was present in 11 of 19 cases. Tracheal tugging occurred in but 2 cases. The earliest and most constant symptoms were dyspnea and cough. Interference with passage of bismuth capsule the size of a quarter through esophagus was found present in every case tested (by X-rays). This is especially valuable in small aneurisms growing back from the transverse part of the arch, as it shows the esophageal obstruction before dysphagia appears. Lange (Lancet-Clinic, Feb. 19, 1910).

The aneurism forms a smooth round or oval enlargement in the course of an artery. It is not sensitive, unless inflamed, is not adherent to the overlying skin, but may be associated with edema and venous congestion of the parts distal to the tumor. The swelling has an expansive pulsation up to the time that a sufficiently thick layer of clot forms within the sac to abolish this sign, so that the symptoms are at times divided into those of the expansile and those of the non-expansile stage. The artery distal to the aneurism gives a retarded and feeble pulse. The expansile pulsation may be less marked and the tumor softer when the parts are elevated. The pulsation is diminished by pressure upon the main artery proximal to the aneurism, and in some cases the sac may then become softer and collapse. On auscultation a systolic or sometimes a double rough murmur or bruit is heard, loudest at the proximal pole. A shadow, emphasized if calcareous deposits are present, may be shown by the fluoroscope or skiagraph.

Subjective symptoms include pain from the stretching and compression of nerves and the arrest of the venous or lymphatic circulation. The pressure and erosion of bone, especially noticed in aneurisms of the aorta, cause the characteristic boring, so-called osteo-

pathic pains which are usually more severe at night.

In the skull the rushing sound and bruit, headache, and the evidences of cerebral pressure or irritation, such as choked disk, vomiting, dilated pupil, motor and sensory disturbances, and localizing nerve palsies, may be present.

> When an aneurism causes paralysis of the third nerve alone, it is uniformly seated upon the trunk of the internal carotid, between the origins of the anterior and posterior communicating arteries. When the aneurism involves the origin of the posterior cerebral artery, the paralysis of the third nerve is accompanied by paralysis of the corresponding facial. The only subjective symptoms (besides the diplopia) are pains in the head and constant noises upon the same side as the aneurism. These cases always end fatally. Pascheff (Archiv d'ophtal., Oct., 1910).

In the neck the situation of the tumor, expansile pulsation, and the effect upon the distal vessels are characteristic symptoms.

In the chest the recurrent laryngeal nerve frequently is involved with the production of rasping voice, spasm or paralysis of the vocal cord, and brassy cough. Pressure upon the sympathetic may produce unilateral sweating and unilateral contraction or dilatation of the pupil as well as tachycardia. Peripheral neuralgia may result from compression of the intercostals. Compression of the phrenic may cause dyspnea and hiccough, while pressure upon the esophagus may result in dysphagia.

> Although there is no one pathognomonic sign of thoracic aneurism, there are certain symptoms and signs taken together which make its existence practically certain. The pain, often slight and not complained of except after particular inquiry, is continuous, is situated near and to the left of the vertebral column, and tends to radiate to the shoulder, the left arm, and the neck. Examination of the chest shows no loss of resonance on the left side, but the resonance is not increased as in pneumothorax. At the same time the breath sounds are diminished over the left lung—this being due to partial compression of the left bronchus. The inspiratory sound is shorter over the left side, the first period of inspiration being inaudible and the air then entering with a rush, as though a valve had been opened. On inspection, there is relative immobility of the left side of the chest, or in some cases there may even be definite retraction. If the above signs be present, together with dyspnea on effort, in a patient whose general health is fairly good and who has no sign of malignant disease, the presumption of the existence of aneurism is strong. Inequality of the pupils is often an early symptom. Clément (Lyon méd., March 31, 1907).

Tracheal tugging is often found in aneurism of the arch of the aorta, and is due to the transmission of the aneurismal pulsations to the left bronchus, and is detected by inclining the head and lifting the larynx and trachea by the finger and thumb caught under the hyoid bone.

> Six cases illustrating the way in which an aneurism of the aorta is liable to push the trachea backward, downward, and toward the left, and thus pull the larynx out of place. This dragging down of the larynx and its deviation to the left and back may, the writer asserts, be regarded as a reliable sign of aneurism of the aorta. Boinet (Bull. de l'Acad. de Med., Dec. 21, 1909).

Inanition may follow in the rare instances in which the thoracic duct is compressed. In thoracic aneurism the distal vessels show a retarded and reduced pulsation, so that the pulse may be weak or even absent from the one wrist.

Case of aneurism of the aortic arch in which the pulse of the carotids and right radial arteries had the reversed character of the pulsus paradoxus. There was a very marked diminution in the volume of the pulse during expiration, and with the respiratory variations there was a definite anacrotic wave. Post-mortem examination showed an aneurism involving chiefly the posterior portion of the aorta in the region of the transverse arch. The left carotid and innominate arteries sprang from the anterior surface of the arch instead of from the convexity, on account of the distention of the aorta. With each expiratory excursion these blood-vessels were compressed against the bony thoracic walls. J. Hay (Lancet, April 27, 1901).

In the course of their studies upon lesions of the aorta the writers have been impressed with the frequency with which some of the lesser signs of aortic aneurism were present. Inequality of the pulse was present in 10 out of 18 cases. In 9 of the 10 cases pulsation was more vigorous on the right than on the left side. Inequality of the pupils was present in 3 cases, but in 1 it might have been due to nervous complications. Suprasternal pulsation was present in 12 cases and absent in 6. Tracheal tugging of distinct downward character was present in 11 and absent in 7 cases. A systolic thrill was felt in the vessels of the neck either with or without slight pressure in 9 cases, and it could not be elicited in 9 cases. A systolic murmur usually transmitted into the vessels of the neck was present in 11 cases, but was not heard in 7. Twelve of the cases had dyspnea; in 1 of these there were physical signs of emphysema and chronic bronchitis; in the others it was probably due to the cardiac condition. J. Sailer and G. E. Pfahler (Amer. Jour. Med. Sci., Oct., 1903).

The arterial blood-pressure in most cases of aneurism of the thoracic aorta or innominate is either normal or slightly above normal. It is, as a rule, however, much higher in cases of mere dilatation of the aorta, and this fact is of some value in the differential diagnosis of these two conditions. Williamson (Lancet, Nov. 30, 1907).

In examining for aneurism of the aorta, one should carefully percuss the area of dullness of the great vessels, note the conduction of the heart sounds in this area, examine both radial pulses simultaneously, examine for the tracheal tug, note all evidences obtained by inspection or palpation, note carefully all the anatomical relations of the aorta, and ever keep in mind the possibility of aneurism. The early symptoms are usually pain or disturbance with the respiratory apparatus, the latter from pressure on air passages or the recurrent laryngeal nerve. The symptoms often simulate those of heart disease. There are no pathognomonic signs; the features may be entirely different in successive cases. Arnold (Amer. Jour. Med. Sci., Apr., 1908).

Case which confirms the possibility of a disconnected respiration of a staccato type from the hammering of the trachea by an aneurism resting against it. Ortner (Med. Klinik, April 25, 1909).

In cases of thoracic aneurism, delay or increased retardation of one of the radial pulses does occur. The same delay may or may not be present in the case of the corresponding carotid pulse. If the idea, based on experimental physics, be correct, that delay of the pulse-wave is only produced as the result of the wave passing through the aneurism, then the phenomenon of delay should be of most important diagnostic aid in the localization of the aneurism. Digital examination is not a reliable test of the presence or absence of delay. The finger may miss the delay when present, and may diagnose it when absent. A more delicate instrument, such as the clinical polygraph, is necessary. Leonard Findlay (Practitioner, Dec., 1909).

Rupture is signalized by pain of sudden onset with shock. The hemorrhage may escape externally through the skin, into the trachea, or into the alimentary

canal; if into the pericardium there are evidences of acute heart compression; if into the cavity of the thorax, of hematothorax; if into the muscular substance, the formation of a progressively enlarging tumor. The rupture may be immediately fatal, or the patient may live for hours or for days, and repeated or continuous leakage may occur. Rarely does recovery follow after an aneurism of one of the great vessels of the trunk has ruptured, although the patient may survive for days or weeks.

> Case of abdominal aortic aneurism in a man aged 41 years in whom the writer observed several hyperesthetic cutaneous zones, as described by Head. Such zones are segmental regions of the body corresponding to the various viscera, exactly at the sensory innervation of the skin, as described by Sherrington, Starr, Kocher, and Thorburn. Trophic disturbances occur in the skin in disease of the arteries, as, for example, in zoster. The points noted in the study of the present case included the belt-like distribution of the radiations of pain due to the abdominal aneurism, these pains dating many years before the development of the symptoms. E. Cedrangolo (Riforma medica, Mar. 23, 1907).

COURSE.—Aneurisms tend to progressively dilate and finally to rupture. In rare instances an aneurismal sac may remain stationary for many years, finally to again progressively dilate. In a third class spontaneous cure occurs by the coagulation of blood within the sac, which may completely consolidate it, with or without obliteration of the arterial lumen. Any condition which interrupts or retards the circulation through the sac may favor this spontaneous cure. This termination at times is followed by a fatal gangrene from obstruction of the collateral circulation.

Plastic arteritis with thrombosis and obliteration of the artery may also lead to a cure. More frequently the aneurism progresses to rupture. The rupture may occur through the skin, mucous membrane, into a serous or synovial cavity or into the subcutaneous tissues, muscles, or fascial planes.

There may be repeated moderate hemorrhages, one or several large hemorrhages, or a rapid hemorrhage sufficient to cause almost instant death or a progressively increasing hemorrhagic edema from a *leaking aneurism.* This may lead to gangrene.

Suppuration of an aneurism occurs most frequently in the axillary region and usually results from the formation of an abscess adjacent to the sac. The sloughing of the sac wall may be followed by great hemorrhage as the abscess opens. Rarely does a plastic arteritis produce clotting and spontaneous cure.

DIFFERENTIAL DIAGNOSIS.—The expansile pulsation, bruit, and retardation of the distal pulse are fairly characteristic symptoms of aneurism. In a consolidated aneurism, or one in which the sac has been filled by clot, these signs may disappear.

The history and presence of a firm mass in the wall of the blood-vessel are suggestive. Tumors and abscesses lying upon large arteries may pulsate, but the expansile type of pulsation is absent.

When the skin over an aneurism has become inflamed the condition may closely simulate an abscess, so that only by a careful study of the patient is a correct diagnosis finally to be made.

Before the consolidation, compression of the main artery proximal to the aneurism may produce a characteristic

collapse of the sac, a cessation of pulsation, and bruit, changes which cannot be produced in vascular sarcomas and other tumors which may simulate aneurisms.

In aneurisms of the thorax X-ray examinations are often diagnostic.

In suspected aneurisms of the abdominal aorta loss or retardation of the femoral pulse should be especially looked for. The marked pulsation of the undilated aorta in thin persons should not be mistaken for aneurism.

In determining the compressibility of the aneurismal sac the greatest gentleness must be employed. We have observed hemiplegia to promptly follow the examination and the palpation of a carotid aneurism for the dislodgment of particles of contained clot.

TREATMENT. — Dietetic, hygienic, and medicinal measures have been used since antiquity with the object of slowing the circulation and so simulating coagulation that a clot would fill the sac. The ancient method of Valsalva included **absolute physical and mental rest,** a very **limited diet, with the deprivation of fluid,** and repeated venesections continued until the patient was too weak to lift a hand.

The more recent method of Tuffnell's was less severe, although rigorous; it consisted of a reduction in the diet and absolute rest in a horizontal position; 2 ounces of bread and butter are given for breakfast with 2 ounces of milk; 3 ounces of bread and butter with 4 ounces of water or claret for dinner; 2 ounces of bread and butter with 2 ounces of tea for supper. A fat diet has been advised by Powell, and the use of meats has been condemned.

> Cure by what was practically the Tufnell treatment. It consisted of as nearly absolute rest as possible, restricted diet for a week and later an ordinary fish diet, no stimulation, and **potassium iodide,** 10 grains three times a day. The dose was quickly and steadily increased so that by the end of the third week 60 grains were being taken three times a day, with no ill effects at any time. As a local application to the swelling, **collodion** was painted all over the surface every night and morning. Instead of continuing his previous downward progress, he commenced to improve from almost the commencement of the treatment, and was discharged apparently cured in six weeks. Young (Lancet, Sept. 22, 1906).

Drugs are employed to reduce the cardiac frequency, to diminish arterial tension, and increase the coagulability of the blood. **Potassium iodide** has been considered to be the most valuable drug. Ten grains three times a day may be increased until 40, 60, or 200 grains three times daily are administered, according to the degree of tolerance. It is especially valuable in syphilitic patients.

> The writer reports the marked success attending the treatment of an interesting and apparently hopeless case of thoracic aneurism which had threatened to rupture externally. The skin covering the tumor, which was located in the median line of the neck, reaching from the level of the lower border of the third rib to just above the level of the lower border of the thyroid cartilage, was extremely thin, tense, and shiny, looking like an abscess on the point of bursting. The patient was put to bed and kept absolutely **quiet.** The **diet** was restricted as far as possible, and all stimulants were withheld. **Iodide of potassium** was administered internally, in doses of 10 grains three times a day, the dose being increased so that by the end of the third week 60 grains were being taken three times a day. **Collodion** was painted all over the surface of the tumor every night and morning. The patient began to improve from the commencement of the

treatment, until in the ninth week he was well enough to assist in the work of the hospital ward. The tumor was very much smaller, there was scarcely any visible expansile pulsation, and the overlying skin was normal. The patient returned to his work. E. E. Young (Lancet, Sept. 22, 1906).

Three cases of thoracic aneurism treated by large doses of **potassium iodide** with excellent results. In 2 cases there was apparent recovery with disappearance of the pulsating tumor and the bruit. The third case was so far advanced that external hemorrhage had taken place from the anterior wall of the aneurism; yet on 80 grains of potassium iodide three times a day marked improvement took place, the patient being enabled to return to business and to lead a quiet life. Failure in the treatment of aneurism with potassium iodide often results from the fact that the dose is too small. Sixty-grain doses are necessary in bad cases. Kingdon (Lancet, Aug. 22, 1903).

To increase the coagulability of the blood in the treatment of saccular aneurisms the subcutaneous injections of **gelatin** were first recommended by Lancereaux and Paulesco. One or 2 Gm. of purest gelatin are dissolved in 100 c.c. of decinormal salt solution, and sterilized by heating to the boiling point for one-half hour on five successive days. Before use the gelatin is warmed to the temperature of the body and 100 c.c. injected under the abdominal skin every two, three, or four days.

The injections are often followed by fever and pain. The possibility of extensive coagulation and of embolism has not been demonstrated. The injections may cause increase of vascular pressure and involve rupture of a large-sized aneurism whose walls are thin. The clinical observations so far made do not warrant an exact estimate of the value of the **gelatin** treatment. Henri Grenet and G. Piquard (Archives générales de méd., June, 1901).

Plea for the use of injections of **gelatin** in aneurism of the aorta. The danger of tetanus is removed if the gelatin is properly sterilized and no disagreeable effects are noticed by the patients. The relief of pain is always very prompt. The injections may be given as high as 5 per cent., although half that strength is usual. Six to 7 ounces are injected at intervals of five or six days. The usual formula is 2½ per cent. gelatin in 7 per cent. salt solution. Lancereaux (Revue de thérap., No. 13, 1906).

Case of large traumatic aneurism occupying the lower half of the left popliteal space, and extending downward to a line about 6 inches below the knee-joint. The dilatation, it was thought, involved the trunk of the posterior tibial artery above the origin of the peroneal branch, and also the lower part of the popliteal artery above the origin of the anterior tibial. An attempt, therefore, to extirpate the sac would have completely abolished the circulation in the leg, and very probably resulted in gangrene. After a prolonged and careful treatment by rest and flexion of the leg, which proved unsuccessful, the author tried repeated subcutaneous injections of sterilized **gelatin** serum. Seven injections were made, the intervals varying from seven to twenty days. After five days after each injection the aneurismal tumor became smaller and firmer. The last injection was followed after an interval of about ten days by complete cure. Le Dentu (Bull. et mém. de la soc. de chir. de Paris, No. 10, 1905).

Several cures have been reported from the use of gelatin, but in other instances undesirable thrombi have formed in the larger veins, while tetanus has followed the use of imperfectly sterilized gelatin. Should the clot which forms in the aneurismal sac soften and be absorbed, the gelatin injections may be repeated with a possibility of good effect.

The internal administration of **calcium chloride** and the subcutaneous

injection of **horse serum** have also been used to increase the coagulability of the blood.

Case of aortic aneurism in which all the symptoms, except a slight headache, had disappeared as a result of the administration of **calcium chloride** for about two months. The calcium chloride was given three times daily. The aneurism was clearly visible under the X-ray. Ambrose (Jour. Amer. Med. Assoc., Oct. 31, 1908).

Arterial Compression.—The object of this method is to so slow the blood-current within the sac that a coagulum may form. The pressure may be proximal to the aneurism and be carried out by means of a pad, tourniquet, or the pressure of the thumbs of assistants acting in relay. The pressure of the thumb is reinforced by a 6-pound weight, and before the thumb of one assistant is removed that of another is properly placed. Each assistant serves for fifteen or twenty minutes, and the treatment is continued for from twenty-four to seventy-two hours. The method by compression is painful and when instrumental may cause sloughing or gangrene. The digital compression requires many assistants and is troublesome, but not so apt to cause sloughing. The compression occasionally cures, but often if the clot is deposited it is dissipated before organization has occurred.

Three cases of aneurism followed, 2 for eight years and 1 for four years, in 2 of which permanent cure has resulted from treatment based on a reduction of vascular tension below the normal. The treatment consists in keeping the patient at **rest** in bed and in prescribing a **diet** from which soups containing an excess of fat; meats, especially those cooked rare; game, fish, cheese, salted foods, tea, coffee, spirits, heavy beers, and an excess of wine are eliminated. Tobacco is also forbidden. Drugs, such as **nitroglycerin** and **sodium nitrite**, were administered. The iodides have been overrated in this connection. In syphilitic aneurisms mercurial injections are dangerous on account of their liability to affect the kidneys, and, as a consequence, to cause increased arterial tension. The **milk diet** in connection with **theobromine**, which assists in eliminating vasoconstrictor poisons, is very helpful in reducing vascular tension. H. Huchard (Jour. des praticiens, Nu. 20, p. 307, 1906).

Forced flexion of the elbow and knee, the part being held by a bandage with the pad at the flexure, has been employed for small aneurisms of the extremities. The position is uncomfortable and the method of little advantage over other methods of compression.

The isolation of a mass of blood within the aneurismal sac by the application of an **Esmarch bandage** below and above the aneurismal sac, while efficient in causing clotting, has led to gangrene of the extremity, and the method has been abandoned. It has been advised that an Esmarch bandage be applied for one and one-half hours and then removed, with continuous light compression of the artery above the aneurism for several days. Apart from the danger of compression, another danger of these methods is in the completeness of the coagulation, which may extend into the collateral vessels and so destroy their function that gangrene follows.

Arterial Ligature.—Ligature of the main artery just above the sac is especially efficient in interrupting the circulation. This is Anel's operation, but was modified by John Hunter, who placed the ligature at a distance above the sac, where he supposed that the arterial walls were healthier. Anel's operation is now preferred to Hunter's.

The most important part of the new surgical work with blood-vessels, especially with aneurism, depends upon the similarity of the serous coat of blood-vessels to the peritoneum. Like the latter, the former throw out lymph for purposes of repair. Irritated surfaces in apposition adhere, and septic processes in the serous coat cause changes similar to those which occur in the peritoneum. Torsion of blood-vessels also causes quick plastic occlusion that arteries of the third class may be thus treated in place of by ligation. Aneurism treated by **digital pressure**, by the introduction of **coils of wire**, or by **electric needles** causes exudation of lymph from the serous coats, followed by adhesion of apposed surfaces. The new work in suturing blood-vessels depends for its safety upon the prompt plastic repair of the serous coats. Morris (Annals of Surg., July, 1908).

When on account of anatomical conditions the ligature cannot be placed above the sac the method of **distal ligation**, such as Basedow's, in which the main vessel is ligatured, or Wardrop's, in which one or more of the chief branches is secured as by ligation of the right subclavian for aneurism of the innominate artery, may be tried. Rarely are they efficient.

Case in which **ligation** of the abdominal aorta was performed for dissecting aneurism involving the wall of the aorta from the celiac axis to the mesenteric vessels. This makes the fourteenth recorded operation in which the aorta has been ligatured. So far they have all proved fatal, but this case is encouraging, as showing that there is no inherent reason why success should not yet be attained. For two days the patient did very well, but on the third day she showed signs of intense septicemia, and she died fifty-three hours after operation. On post-mortem examination, it was found that the septicemia was due to gangrene of small portions of the bowel, which had lain in contact with the forceps used to clamp the ligature. The aneurism was found to be full of blood-clot, while the aorta remained patent. An embolus was found in the left internal iliac. The case demonstrates that an aneurism of the aorta can be made to fill with clots by the application of a temporary ligature to the aorta, and that circulation in the extremities may be re-established on removal of the ligature. R. P. Morris (Annals of Surg., Feb., 1900).

Ligation of abdominal aorta has been done 14 times to relieve a peripheral aneurism. It makes great demands on the heart and has never been successful. Collateral circulation soon developed, annulling the benefits of the ligation. The great number of communications with the general circulation render the establishment of collateral circulation inevitable. Its development, however, requires extra work on the part of the heart, thus inducing considerable hypertrophy. In the absence of general atheromatosis of the vessels and if the operation is technically possible, extirpation of the aneurism may be successful. In 10 of the 14 cases on record death was the direct result of the operation. Katzenstein (Archiv f. klin. Chir., Bd. lxxvi, Nu. 3, 1905).

A successful case (the ninth with recovery) of **ligation** of the innominate artery. The patient was a colored man aged 27 suffering from subclavian aneurism; the innominate only was tied with a largest-sized braided silk ligature in a "granny" knot drawn just tightly enough to approximate the vessel walls, but not to crush its coats. The ligature came away fifty-one days after the operation while the wound was being dressed; the recovery was good practically in twenty days. W. B. Burns (Jour. Amer. Med. Assoc., Nov. 14, 1908).

Dix's Operation.—The artery is exposed and encircled by a strand of silver wire. The ends of the wire are brought through the tissues to one side of the wound, and are twisted over a

split cork until pulsation ceases in the aneurism. Later slight pulsation returns to the sac, and after two or three days the wire is tightened by placing wedges under the loop. About the fifth or sixth day the wire is cut and removed.

Excision of the Sac and Implantation.—The interposition of a segment of an adjacent vein has also been tried, but the procedure has rarely been successful.

Removal or Obliteration of the Sac.—The ancient method of Antyllus, in which the sac was dissected out or opened and packed, has been succeeded by the modern **obliterative method of Matas.** In this operation the patient is anesthetized, a tourniquet applied, the sac is opened by a longitudinal incision, emptied, and the mouth of each vessel is exposed within the sac and sutured from the inside by separate silk or chromicized catgut sutures. The redundant walls of the sac are then so enfolded and sutured as to form a solid pad under the skin. The advantage of this method lies in the fact that the sac is not loosened from the adjacent tissues, and, therefore, there is little risk of injuring adjacent collateral nerves and veins.

Matas's method combines the advantages of ligation and excision, while at the same time it is easier, safer, and may be more conservative. It is suitable both in the fusiform and sacculated types of the disease. After applying a constrictor above the site of the disease, if in a limb, or temporarily ligating the proximal and distal trunks, if the carotid is the vessel at fault, the operator cuts into the sac, thoroughly removes the contained clots, rubs the serosa with gauze, and proceeds to insert sutures. The sutures, preferably catgut, are first applied to the openings of all vessels entering or leaving the sac; then the deeper portions of the sac are closed by two rows of continuous Lembert sutures. The elastic constrictor is now removed, and if any blood escapes one or two points of suture are inserted to control this. The next step consists in folding the excess of sac wall on itself, and in so doing inverting the edges of the skin wound. The operation thus performed has been very successful, and in some cases of sacculated aneurism the circulation may be re-established through the repaired vessel. Binnie (Jour. Amer. Med. Assoc., June 25, 1904).

Two cases of fusiform aneurism rupturing into the surrounding tissue and treated by the writer by **Matas's method** of suturing the leading openings within the aneurismal sac. In neither case was the sac obliterated, but drainage was employed and the results were satisfactory. In one of his cases to have sutured together the walls of the cavity would have required a 14-inch incision. It is better in such cases to close the incision partly and to drain, allowing the cavity to fill up by granulation, instead of closing it by suture, as is done in the unruptured cases. J. A. Danna (Jour. Amer. Med. Assoc., Aug. 5, 1905).

Matas's method approaches nearer the ideal for the cure of aneurism than any other, and is more generally applicable. It can be employed in every accessible variety in which the circulation can be temporarily controlled, and it interferes less than any other with the blood-supply beyond the aneurism. The experimental work of various surgeons shows the possibilities of vascular surgery, suture, anastomosism transplantation, substitution of vein for artery, arteriotomy for embolism having all been found practicable. The operation of Matas was based upon the fact that when intima is approximated to intima union occurs, and, hence, that an aneurism could be cured by closing the mouths of the vessels entering it and obliterating the sac by approximating its walls. Gibbon (Annals of Surg., Sept., 1907).

Results of **endoaneurismorrhaphy** (the writer's method) in 85 operations

by 52 surgeons up to the present date. The legitimate mortality of the operation itself was 2.3 per cent.; of secondary hemorrhage, 2.3 per cent.; of gangrene, 4.6 per cent. Eliminating 3 of the gangrene cases in which there was simultaneous injury and ligation of veins or secondary ligature of an artery, the percentage of this accident is 1.1 only. The total of postoperative deaths from all causes was 7 to 78 recoveries. The percentage of relapses, which occurred only in the reconstructive operations (4 in 13, or 28 per cent.), was only 4.7 per cent. to the total. The author believes that the fundamental principle on which the operation is based, viz., that the endothelial lining of the vascular system which is continued in the aneurismal sac is analogous in its pathological behavior to the reactions and reparative processes which occur in the endothelial surfaces of the other serosa, such as the peritoneum and the pleura, has been absolutely confirmed by the experience in these 85 cases. They have also disproved Scarpe's law that complete obliteration of the vessel is an essential to the cure, which result is also supported by the facts of the suture and repair of arteries. An important point of the technique is the prophylactic hemostasis, which must be made absolute, and the problem increases in complexity and difficulty the higher the operation, and the writer mentions the methods and appliances for this purpose. Experience demonstrates that in all sacciform aneurisms with a single orifice of communication the closure of this orifice by suture without interfering with the lumen or the capacity of the vessel is to be looked on as obligatory. The indication for the reconstructive operation, however, is fusiform aneurism with separate orifices of entrance and exit, and must still be considered *sub judice*. In the vast majority of cases of aneurism of the extremities the simple obliterative procedure proved satisfactory. It gives a cure with less risk to the distal parts than either the ligature or the method of extirpation. The indications in any given case will not be entirely satisfactory until we have a sure clinical proof of the adequacy of the collateral circulation. Korotkow's method of testing the most peripheral blood-pressure may be the solution of the problem. R. Matas (Jour. Amer. Med. Assoc., Nov. 14, 1908).

The advantages of **Matas's endoaneurismorrhaphy** are as follows: It is more radical in its effects than ligature and extirpation; it is free from risk of injury; it is only exceptionally followed by gangrene; it does not interfere with the collateral circulation; it prevents any danger of injury of a vein, and is applicable to cases in which extirpation is no longer possible. For suture chromicized catgut or fine silk is employed. The method is chiefly indicated in cases in which provisional hemostasis can be carried out and where the aneurismal sac is accessible. Altogether 149 cases have been reported, in 131 of which the lower extremity was affected. Among the last 64 cases there have been no deaths, no recurrences or secondary bleeding, and only one instance in which gangrene occurred as a complication. F. Gardner (Gaz. d. Hôp., No. 118, 1910).

A second method is **Matas's conservative endoaneurismorrhaphy,** to be used for sacculated aneurisms opening by a narrow mouth into the main vessel. This opening is sutured from the inside of the sac and the wound reinforced, pleating and suturing the overlying sac. In reconstructive endoaneurismorrhaphy an attempt is made to restore the normal lumen of the artery in a fusiform aneurism. A rubber tube may be temporarily introduced as a guide between the afferent and efferent mouth of the sac, and the walls of the sac so sutured as to restore a canal having the lumen similar to that of the adjacent artery. This line of suture is likewise to be reinforced by pleating and suturing the redundant walls of the sac.

Temporary partial obliteration of the main artery by use of **metallic rings or clips**; Halstead and others have devised rings or clips composed of aluminum or other metal which may be applied to an arterial trunk in such a manner that the lumen in the vessel is reduced or obliterated. By reducing the lumen the current in the artery and sac distal to the ring may be so slowed as to favor curative coagulation, and if properly applied it has been found that these rings are well tolerated by the arterial wall, and have not the same tendency to ulcerate into the lumen of the vessel as a ligature.

> The pain of an abdominal aneurism may be greatly lessened and its growth checked by the application of a partially occluded **metallic band** to the aorta, proximal to the aneurism. When the aneurism is saccular and gives origin to no important vessels a cure is possible by this means. When the band produces an anemia of the kidneys, there appear for a time large numbers of waxy casts in the urine. Gatch (Annals of Surg., July, 1911).

The application of a ligature is not feasible in the case of the aorta, for in every case in which a ligature has been employed the patient has died, if not from the immediate danger from the operation, then some days or weeks later from secondary hemorrhage due to the ligature cutting its way through the wall of the artery.

Macewen's Acupuncture. — This method aims to scarify the lining of the sac so that the granulations form upon which the blood may coagulate. One or more long fine-silk needles are thrust into the aneurism so that their points just touch the opposite wall. The pulsatile movements of the sac wall cause the needle-points to scratch the lining of the sac. The needles may be left in place for some hours, attempts being made to so change their position that as large an area as possible of the lining will be abraded. The method is of very limited value.

Electrolysis increases the efficiency of Macewen's method. Insulated needles are passed and a galvanic current from 20 to 30 milliampères. Needles should be permitted to touch the opposite wall of the sac so as to produce the delicate abrasion as in acupuncture.

Moore's method consists in the use of a delicate wire so tempered as to coil within the sac, where it is permitted to remain permanently. A small, hollow needle is introduced into the sac until the blood flows and from 5 to 20 feet of wire, according to the size of the sac, passed through the needle. The end of the wire is then pushed through the needle or cut close to the skin and made to imbed itself.

The **Moore-Corrady method** consists in passing the current from 20 to 80 milliampères through the coil of wire which has been introduced into the sac. A wire of fine drawn gold is preferred, and from 5 to 20 feet introduced, as in the Moore method. The current is permitted to flow about one hour, negative pole being connected with a pad upon the patient's abdomen or back. The wire is permitted to remain permanently within the sac.

> Aneurism of the left subclavian artery in which 20 feet of **gold wire** were introduced into the sac through a hollow needle, and a **galvanic current**, gradually increasing from 1 to 80 milliampères, was employed for about one hundred and ten minutes. The pulsation and size of the tumor temporarily decreased and afterward increased, and death occurred on the twentieth day after operation, due to exhaustion produced by long-continued pain, and hastened by the formation of a thrombus in the left common carotid artery,

caused by the pressure of the aneurism. The necropsy showed a cocoanut-shaped aneurism involving the entire length of the artery. Its cavity was occupied in large part by a clot in varying stages of organization, through which the wire was well distributed. This operation is worthy of trial when medical treatment fails. The percentage of success will be greatly increased if the operation be not performed as a last resort. Daland (Penna. Med. Jour., Dec., 1903).

These methods have chiefly been employed for aneurisms of the thoracic aorta. Occasionally cures are reported, but failures are frequent and fatal accidents have occurred. It is obvious that even in so-called cures the patient's ultimate condition is not a normal one. Sterilized horsehair, silk, and catgut have also been tried, but with questionable benefit.

A recent addition to the methods of treatment is that of Abrams, which, though qualified by him as palliative, seems to have produced lasting beneficial effects in a large number (40) of his cases. It consists of **repeated concussions over the seventh cervical vertebra,** which are thought by Abrams to cause, through the vasomotor system, contraction of the diseased vascular area. Confirmatory evidence is still too scant to warrant any opinion as to the actual value of this method.

A. Abrams, of San Francisco, claims that the subsidiary center of the vasoconstrictor nerves of the aorta is located in the spinal cord in proximity to the spinous process of the seventh cervical vertebra, and that by stimulation of the center in question by concussion the normal as well as the abnormal aorta may be brought to contraction. Ample evidence is furnished of the latter fact in his work on spondylotherapy. The method, in brief, which he suggests in the treatment of aortic aneurism consists in **concussion of the spinous process of the seventh cervical vertebra.** He deprecates the employment of the conventional vibrating apparatus. The vibratory apparatus which the physician must employ is one giving the percussion stroke. All other motions, such as oscillations, shaking, and friction, interfere with results. In the absence of a suitable apparatus, a pleximeter (a strip of linoleum or thick rubber) and a hammer, to the end of which is fixed a piece of hard rubber, are employed. The pleximeter is applied to the seventh cervical spine and is struck a series of rapid and moderate blows by the hammer. The daily *séances,* according to results, may last from five to fifteen minutes, but during the *séance* the treatment must be interrupted from time to time to avoid irritations of the skin.

The results of Abrams's method are usually immediate, great relief following a few *séances.* When the writer first encountered the monograph of the latter on the subject, he was rather skeptical, although Abrams anticipates such criticism in his book by observing that any merit attached to his method may be obscured by its simplicity.

The writer presents the history of a personal case suffering from aneurism of the thoracic aorta which was treated successfully by the "concussion method" of Abrams. The aneurism had perforated the chest wall. Within one week all the symptoms had disappeared, and fourteen months after the patient's discharge he was as well as when dismissed. L. St. John Hely (Amer. Jour. of Physiol. Therap., July, 1910).

Case of aneurism of the thoracic aorta treated by **Abrams's method.** After the first daily *séance* of concussion, lasting ten minutes, the systolic murmur over the aorta almost disappeared. Three days later the aneurismal dullness measured transversely 2.6 cm. After two more days the aneurism measured 2 cm. and the patient's weight was 123 pounds, an increase of 5 pounds. Two days later there was absolutely no dullness over the site of

the aneurism, the pains in the chest were gone, expectoration was reduced about 50 per cent., but the cough continued with less frequency and severity. After about two months the patient's weight was 135 pounds. He had absolutely no symptom beyond an occasional slight cough. Turnbull (Med. Record, Sept. 9, 1911).

Report of a case of aneurism of the thoracic aorta treated successfully by **Abrams's method.** There was no X-ray verification of the condition in this case, but the physical signs respecting the aneurism and the results of treatment were absolutely positive and unmistakable. L. C. Boyd (N. Y. Med. Jour., Oct. 21, 1911).

ARTERIOVENOUS ANEURISM.—These conditions, termed by Hunter aneurism by anastomosis, are characterized by an arteriovenous fistula. They may be divided into two chief forms:—

(*a*) **Aneurismal varix** is characterized by the direct communication of the artery with the vein. The blood-pressure is much higher in the artery; the arterial flow is forced into the vein, which becomes thickened, dilated, sacculated, and tortuous. The condition is usually due to the incised wound involving the contigous walls of an artery and vein, and gunshot wounds. Occasionally they result from contusions without external wound, and may even develop spontaneously. In the older days the common cause was phlebotomy. In order of frequency the brachial, femoral, popliteal, carotid, temporal, subclavian, and axillary arteries are involved. Instances are recorded in which the condition has spontaneously occurred in connection with the abdominal and thoracic aorta, and after gunshot wounds of the head a fistula may form between the cavernous sinus and internal carotid artery.

(*b*) **Varicose Aneurism.**—The vein communicates with the artery through the medium of an aneurismal sac. This usually develops from a traumatic aneurism which becomes adherent to an adjacent vein and finally opens into it. Both the artery and the vein may be injured simultaneously and an intermediate blood-clot first form, the sac finally replacing the area occupied by the blood-clot. Such an aneurism may form at the ends of the divided vessels in an amputation stump.

An arteriovenous aneurism with an arterial sac, such as that developed from the erosion of a true aneurism through the wall of an adjacent vein, is rare, and has been classified as a third variety of arteriovenous aneurism.

Symptoms.—A marked pulsation which is communicated widely to the communicating veins is present and usually associated with a loud, whistling bruit. The bruit is both systolic and diastolic. The thrill may be palpable. The interference with the normal circulation in the vein may produce stagnation, local cyanosis, pigmentation, eczema, elephantiasis, muscular atrophy, ulceration, rarely gangrene. The pressure upon the nerves may result in paresthesia or paralysis.

Treatment.—The treatment of arteriovenous aneurism is usually operative, as the disease is usually persistent and progressive. The artery may be clamped above and below the opening and the opening in the artery and vein closed by arterial suture. Where a thoracic aneurism is present the sac may be split and the communicating opening sutured from within the sac, as in Matas's aneurismorrhaphy. In some cases it may be necessary to ligate the artery above and below the point of communication. As a rule, the vein should not be ligatured.

In small traumatic aneurisms in which the distended inner coat of the vessel bulged through the external coats we have found it possible to reduce the hernia-like protrusion and to reunite the median adventitia by fine silk sutures, which reinforce the union by suturing adjacent connective tissue to the arterial wall.

The difficulties which accompany the operative treatment of arteriovenous aneurisms of the subclavian artery are very great. It is not easy to work under the subclavian in the presence of an hematoma. In 4 of the cases the clavicle was resected. The effect upon the arm of the diseased side when deprived of the support of the clavicle and of the blood-supply from its artery and vein must be considered. Another difficulty consists in the size of the vessels and in their situation. Hemorrhage is of grave significance, on account of its profuseness, its frequency, and its depth. In 3 of the cases the sac was opened in order to attach hemostatic forceps. In this location, one should also fear the entrance of air into the veins. The radical operation ought, therefore, to be rejected as an operation of choice, on account of the dangers of the operation. Even if the operation should not result fatally, the subsequent condition of the patient may be a distressing one, as it was in 2 of the 4 patients who recovered. Pluyette and Bruneau (Revue de chir., July, 1905).

Analysis of 161 cases of arteriovenous aneurisms published since 1889. The femoral was involved in 80 and the popliteal in 35 cases. Much better results are obtainable, as a rule, from operating directly on the sac than from ligatures. The main drawback to a complete cure is the frequent coexistence of nervous lesions complicating the aneurism, which are generally solely responsible for the postoperative disturbances. Only when direct action on the sac is impossible should ligatures be given the preference. Removal of the sac offers the same advantages over incision for the arteriovenous as for the arterial aneurisms. Monod and Vanverts (Revue de chir., Oct., 1910).

Conditions related to aneurisms include certain nevi, cavernous angioma, aneurism by anastomosis, and arterial angioma or cirsoid aneurism. These conditions suggest new growths or tumors more than aneurisms. Some are congenital; others are acquired, and the aneurism by anastomosis, a vascular tumor consisting of involved arteries, veins, and capillaries, which may reach an enormous size, is present. The arterial angioma or cirsoid aneurism usually occurs upon the head about the time of adolescence. It may be congenital or follow traumatism. The arteries are enormously dilated and very tortuous; the bruit may be so loud as to interfere with the patient's sleep. These conditions are usually treated by **electrolysis, ligation,** or **excision.**

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ANGINA LUDOVICI. See Pharynx and Tonsils, Diseases of.

ANGINA PECTORIS. — DEFINITION. — Angina pectoris (stenocardia, breast-pang) is the name given to a group of symptoms which usually depends upon organic disease of the heart or aorta. An attack consists in the sudden onset of agonizing pain in the precordial or sternal regions, accompanied by a feeling of constriction and in severe cases by a sense of impending death. The pain radiates into the back, the shoulders, and the arms, particularly the left. The patient is pale, haggard, motionless, and often bathed with cold perspiration.

SYMPTOMS.—Suddenly, after exertion, excitement, or a hearty meal,

the patient feels an excruciating, burning, or tearing pain in the heart or beneath the sternum, accompanied with a sense of constriction (*angere,* to throttle), as if the heart were in a vise. The pain radiates into the back, upward into the shoulders, and down the left arm, often even to the fingertips. It may be felt in both arms, in the neck and head, and even in the trunk and lower extremities. "In true angina the seat of the pain may be entirely away from the chest, and may be, as in Lord Clarendon's father, at the inner aspect of the arm, or about the wrist, or in rare instances confined to the side of the neck, or even to one testis" (Osler). After an attack, there may be tenderness above and outside the left nipple and in the left arm.

The pain is explained by James Mackenzie as a sensory reflex due to irritation of the 1st, 2d, and 3d dorsal and 8th cervical nerves, and the sense of constriction to reflex stimulation of the intercostal nerves.

Paroxysms occur in which pain is slight or absent (angina *sine dolore*). Early attacks are often of this sort. Later on there may still be no pain, or the paroxysms may sometimes be painful and at other times not.

A feeling of numbness accompanies the pain. There is a sense of impending dissolution. The sufferer sits or stands immobile and hardly dares to breathe. Yet there is no real dyspnea. The face is pale or livid; the forehead wet with perspiration. The pulse may remain strong and regular. Usually it is accelerated and of increased tension. A pulse of habitual high tension may be somewhat lowered during the attack (Mackenzie). The pulse may intermit or vary. Exceptionally it is slowed. The paroxysm lasts a few seconds or minutes,—sometimes half an hour or even several hours. At the end of it the patient often belches gas or vomits or has a movement of the bowels, with great relief. The inference that indigestion has caused the paroxysm is natural, but probably erroneous; although it is true that even slight exertion directly after a meal may precipitate an attack.

Study of 21 cases. The attacks usually came on after a meal. In every case exertion increased the pain, and the sense of fullness was relieved by the eructation of gas. Most of the patients attributed their trouble to indigestion. In all there was shallow respiration with an occasional deep inspiration. The heart's action was usually slow, occasionally palpitating or irregular, and the pulse was generally tense and sustained. In all, arterial fibrosis could be recognized by a thickening of the palpable arteries; cardiac disease manifested by accentuation of the second aortic tone, feebleness of the first sound, cardiac murmurs, etc., was present at some time in nearly all cases. During the attacks the second aortic sound was always much accentuated, while the first sound could be heard very indistinctly. Frank Billings (Chicago Medical Recorder, Feb. 1901).

Case in which the symptom-complex of angina pectoris showed none of the ordinary causes, namely, syphilis, alcoholism, nicotinism, or excessive exertion. In addition to excessive mental toil and excitement due to the patient's occupation, and the occurrence of rheumatism nearly half a century before, the only factor of importance was the habitual bolting of large quantities of food rich in proteids and carbohydrates, producing a marked disturbance of metabolism, as evidenced by the occurrence of indicanuria, acetonuria, and intercurrent glycosuria in quantities as great as 8 per cent. Daland (N. Y. Med. Jour., May 20, 1909).

The attack may prove immediately fatal. If not, the patient is left exhausted, but regains his usual condition in a few hours or days.

The attack is almost sure to be repeated. This may happen in an hour or not for weeks or months. The length of the interval depends greatly upon the persistence of the patient in avoiding the exciting causes. After a severe attack, rest in bed is desirable for several days, or, if the patient is much enfeebled, for a week or two. Successive paroxysms occur with gradually increasing readiness.

> The body position is of diagnostic value, *i.e.*, retroversion, with the head and trunk extended, the whole body being fixed in this attitude. Not every case assumes this position, but it is sufficiently constant to be an aid in the differential diagnosis in the various types of spasmodic dyspnea—for example, in asthma or uremia; so that in addition to the two cardinal symptoms of pain and anguish he would add a hyperextended position of the head and trunk. This attitude was exemplified in the six personal cases. Minervini (Riforma medica, Nov. 18, 1905).
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> The diagnosis of angina pectoris, at least in its milder form, cannot be made from the history alone. The other forms of cardiac pain, of toxic or neurotic origin, the latter especially in women, may exactly simulate a true angina pectoris. After allowing due weight to the age, sex, and detailed history of the patient, it is necessary to ascertain the presence or absence of signs of organic disease at the root of the aorta. On this hangs an enormously important decision. When plain signs of general arterial or aortic disease coexist with a history of precordial pain there need be no hesitation in making a positive diagnosis of true angina pectoris. But it is otherwise in patients with cardiac pain in whom, as may happen, the accessible arteries are soft, and who do not present signs of gross aortic or pericardial lesions.
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> In diagnosing between true and false, organic or functional, there is one physical sign which the writer believes positive. It is so slight, and apparently so insignificant, that one almost hesitates to mention it. It is simply a slight clicking sound, of a harsh or rough quality, accompanying, or following at barely perceptible interval, the sound of aortic closure. It is not an accentuation of the closure sound of the valve, such as the loud, clean, "cork and bottle" aortic second sound, which is significant of high arterial tension. G. R. Butler (Archives of Diagnosis, Oct., 1909).

DIAGNOSIS.—In true angina pectoris skilled observers almost invariably find evidence of organic cardiac or aortic lesion. In a supposed case these should be sought most carefully. Particularly to be looked for are arteriosclerosis, hypertrophy or dilatation of the left ventricle, aortic regurgitation, and feebleness of the muscular power of the heart.

> The great fact in this disease is the existence of pain around which the attendant phenomena are grouped. It usually radiates to one or both shoulders and arms. There are usually repeated paroxysms induced by exertion or by digestive conditions. Other sensations are faintness, weakness, and breathlessness. Objectively, there are pallor or cyanosis, immobility or contortions, dry or moist skin. The vascular tension varies within wide limits, and there may be an increased flow of urine and saliva. G. A. Gibson (Practitioner, Sept., 1906).
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> When angina pectoris is well characterized, it can be differentiated in a decisive way from the false variety by the angor animi and the strong sense of imminent dissolution. Many additional symptoms may be associated during the paroxysms, but are not necessarily present, and only serve to corroborate the diagnosis of true angina. Among these are: Respiratory disturbances,

including asthma, dyspeptic symptoms; and vasomotor disturbances, such as pallor of the face (rarely lividity), sweats, and coldness of the surface. Anders (Jour. Amer. Med. Assoc., Nov. 3, 1906).

Intercostal neuralgia causes pain along an intercostal nerve, not radiating as in angina pectoris. It presents points tender to pressure near the vertebræ and sternum and in the axilla. It is not associated with disordered circulation. It is more common in women than in men.

Gastralgia is apt to occur when the stomach is empty. The pain does not stream into the shoulder and arm. While there may be collapse and a sense of impending death, there is no evidence of heart disease. Like intercostal neuralgia it is likely to occur in anemic young women, rather than in middle-aged men.

On the other hand, the pain of true angina pectoris may be felt lower down than the precordia. And, as already stated, the termination of an attack may be marked by the discharge of gas. Particularly if there is no extreme cardiac pain, this may lead the patient, and in some instances has led his physician astray.

Cardiac asthma is dyspnea due to a weak heart and occurring more or less paroxysmally. Pain is not prominent. The picture is apt to include pulmonary edema, enlarged liver, and dropsy, and it could hardly be mistaken for angina pectoris. Mitral disease is not apt to be associated with angina pectoris, and relief from attacks is often experienced when a mitral leak develops in an aortic case.

The recognition of cardiac lesions observed after attacks of angina pectoris is of great importance, inasmuch as it leads the physician in charge to insist on perfect rest for the patient for days or even weeks after a severe attack, and thus prevents, in some instances, sudden death. The cases in which the attacks are followed by the appearance of clinical signs in the heart may be divided into three classes. In the first group there is a rise of temperature and a slight enlargement of the cardiac area of dullness. The fever may be slight, but if other causes are excluded it is of great value in the diagnosis of myocarditis following angina pectoris. In the second group there is, in addition to fever, a distinct dilatation of one or other of the cardiac cavities, which can readily be discerned on physical examination. Finally, in the third group, there develops an acute endocarditis following an attack. In spite of the fact that clinically the occurrence of acute endocarditis after angina pectoris is not a well-recognized phenomenon as yet, it has long since been described pathologically. Kernig (Roussky Vratch, Oct. 30, 1904).

"Pseudoangina."—Pseudoangina pectoris, or hysterical angina, occurs in females or neurasthenic men, usually under the age of 40, without evidence of organic cardiovascular changes. There are low tension, feeble second sound, and soft arteries. The attacks are spontaneous and are apt to be nocturnal and periodic (menstrual). They last an hour or two, being more prolonged than the true paroxysms. The patient is agitated, writhes, or walks about the room, and talks. The heart feels not constricted, but distended. The pain is not apt to be so severe as in true angina pectoris. Paresthesiæ and vasomotor symptoms are prominent. The patient's symptoms are sometimes colored by his having consulted encyclopedias and the like (Broadbent). Death never occurs.

Angina pectoris in its typical form is a rare disease. Pseudoangina, or cardiac asthenia, as it is frequently called, is much more common. It is erroneous to speak of angina pectoris as a neurosis of the heart, as in the great majority of instances there are organic changes in the coronary circulation, the cardiac muscle, or lesions of the aortic orifice. Neurotic angina is exceptional, is almost always associated with spasm, or with a sudden increase in intracardiac pressure. Beverly Robinson (Amer. Jour. Med. Sci., Feb., 1902).

Painless angina is much more common than one would suppose it to be from the infrequency with which it is mentioned; but, in all probability, the disease is not always recognized, and the patient's sufferings are attributed to hysteria or some reflex disturbance. When the symptoms are accompanied by a dilated right heart or distinctly atheromatous changes the diagnosis is easy, but when physical signs are absent it is difficult to arrive at an absolute opinion. If, when free from the paroxysms, the patient continually suffers from a feeling of weight or distress over the precordia, and has a tendency to take occasional deep inspirations, there is a strong probability that the right ventricle is affected, and this amounts to certainty if the symptoms are invariably produced or aggravated by exertion. This form of angina is entirely different from the painful variety, and in many instances demands a diametrically opposite treatment. W. W. Kerr (Jour. Amer. Med. Assoc., May 29, 1909).

Hysteria.—It should, of course, be remembered that hysteria may be combined with organic disease, and that a careful physical examination should be made in any suspected case; but the discovery of mitral disease would not be inconsistent with a diagnosis of pseudoangina.

There is a nervous form of syphilitic angina which is distinct from hysterical angina pectoris. The two conditions may be distinguished as follows: In hysterical angina the attacks come on, as a rule, at night; on examination there are found hysterical areas on the skin of the chest, and the attacks begin with paresthesia of such an area, and end in tears, sobs, and other manifestations of excitement. The syphilitic attack of the nervous type is preceded by fatigue, not by excitement. It is very important to distingish the nervous syphilitic type from the organic syphilitic angina, which depends upon a lesion of the heart muscle itself. The chief characteristic of these is the presence of periodic attacks of angina with dyspnea between the attacks. M. J. Breitman (Vratch, Nov. 14, 1900).

Hysterical angina pectoris is common, especially before the age of 40. It is most frequent in women. The crises in childhood are less severe than those of adult life. Almost anything may be the cause of the attack, even acute articular rheumatism. Frequent paroxysms are often noted about the menopause. Sometimes an attack occurs by suggestion from seeing a paroxysm in another. There is precordial pain, often with a distinct aura. The paroxysms occur at night, periodically. About the precordia is generally found an area of marked hyperesthesia. Palpitation, rapid pulse, and vasomotor symptoms are common. In fact the symptomatology is polymorphous. In some cases true aortitis or endocarditis may exist, yet the attacks of angina pectoris are hysterical. Mercklen (Médecine moderne, Apr. 23, 1902).

Syphilis.—A history of syphilis in a man, even if under 40 years of age, renders the occurrence of true angina pectoris less improbable than it otherwise would be, for there is a possibility of syphilitic aortitis obstructing the orifices of the coronaries.

Tobacco, Tea, etc.—Excess in tobacco (less often alcohol, tea, and coffee) and lead poisoning may occasion spurious angina, or again they may aggravate a genuine paroxysm depending on organic lesions.

While certain cases are evidently true angina and others equally obviously pseudoangina, some are extremely puzzling. All these attacks (true and "false") have this much in common, that for the time being the heart is unable to perform the work demanded of it; so that they differ more in etiology and prognosis than in immediate condition.

ETIOLOGY.—Males over 40 years of age in comfortable worldly circumstances make up the majority of sufferers from angina pectoris. Predisposing causes are: alcohol, syphilis (arteriosclerosis, tabes dorsalis), rheumatism, gout, diabetes, chronic nephritis, and bacterial infection (influenza, plague, malaria). Sometimes attacks are hereditary.

As exciting causes may be named: physical exertion, mental strain, profound emotion, and digestive disturbances. The attacks may come in the daytime, especially at first; but some of the worst occur at night; so that finally the patient may dread going to sleep.

> Angina pectoris and the menopause. Attacks of angina pectoris observed for the first time at the menopause may be dependent upon the changes occurring at this period, or they may accidentally begin at this time from other and unassociated causes. In the former case the attacks may be purely neurasthenic or hysterical, or they may be of vasomotor origin (spasm of the coronary arteries), giving the picture of severe organic angina pectoris. These two forms may, of course, be combined. T. K. Geisler (Vratch, Feb. 12, 1900).
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> All cases of angina pectoris are of toxic origin, and the so-called coronary angina is a toxic neuralgia or neuritis of the cardiac plexus, due to uremia, and to be forestalled by the same regimen as uremia. Gilbert and Garnier (Presse médicale, Oct. 13, 1900).

The writer has notes of 268 cases in all—231 men, 37 women. If we recognize a mild neurotic or pseudoneurotic and a grave organic or true form, there were, of the former, 225, and, of the latter, 43. The writer omitted *les formes frustes* unless a patient had subsequent severe attacks. Of the severer form of 225 cases, there were only 14 women. On the other hand, of the minor type, of 43 cases there were 23 women. The age incidence is late, the largest number of cases occurring in persons over 50. Of the 612 deaths in England and Wales, only 36 occurred between the ages of 35 and 45, while between 45 and 65 there were 291 deaths. In Osler's list the age was much the same. There were, under 30 years of age, 9; between 30 and 40, 41; between 40 and 50, 59; between 50 and 60, 81; between 60 and 70, 62; between 70 and 80, 13, and, above 80, 3. In women the age incidence is, on the whole, a little lower than in men.

A point that stands out prominently in the writer's experience is the frequency of angina pectoris in physicians. Thirty-three of his patients were physicians, a larger number than all the other professions put together. Only 7 were above 60 years of age, one a man of 80, with aortic valve disease. The only comparatively young man in the list, 35, was seen nearly twenty years ago in an attack of the greatest **severity.** Worry and tobacco seem to have been the cause. He has had no attack now for years. Two cases were in the fourth decade, 13 in the fifth, and 11 in the sixth. Neither alcohol nor syphilis was a factor in any case; of the 26 patients under 60, 18 had pronounced arteriosclerosis and 5 had valvular disease. In a group of 20 men, every one of whom Osler knew personally, the outstanding feature was the incessant treadmill of practice, and yet every one of these men had an added factor, worry.

So far as symptoms are concerned, the writer's cases fall into three groups: 1, *les formes frustes;* 2, mild, and, 3, severe.

1. The mildest form, *"les formes frustes"* of the French, with substernal tension, uneasiness, distress, rising

gradually to positive pain, is a not infrequent complaint, one, indeed, from which few escape, is associated with three conditions. Emotion is the most common and the least serious cause.

2. Under the mild form, angina minor, come 43 cases. Osler has grouped under these the neurotic, vasomotor, and toxic forms, the varieties which we formerly spoke of as false, or pseudo-, angina. The special features of this variety are: the greater frequency in women, the milder character of the attacks, and the hopeful outlook.

3. Severe angina, angina major, is represented by 225 cases, of which 211 were in men. Two special features here are, existence in a large proportion of all cases of organic change in the arteries and liability to sudden death. Osler (Jour. Amer. Med. Assoc., from Lancet, Mar. 12, 1910).

PATHOLOGY.—It is exceptional for attacks of true angina pectoris to be observed in persons presenting no evidence of organic circulatory lesion. The commonest underlying conditions are sclerosis of the coronary arteries, degeneration of the myocardium, cardiac hypertrophy, atheroma of the aorta, aneurism of that vessel near its origin, and aortic regurgitation. There is, however, "hardly an affection of the walls or cavities of the heart, scarcely a morbid condition of the arteries that nourish it or spring from it, with which the distressing malady has not been observed to be associated" (Da Costa).

Recent writers lay stress on obliteration of the lumen of the coronary arteries as the essential basis of true angina pectoris, which obliteration may be occasioned either by sclerosis of the vessels or by changes in the aorta at their origin. "So intimately associated is the true paroxysm with sclerotic conditions of the coronary arteries that it is extremely rare apart from them" (Osler). Huchard held the same view.

The fact that angina pectoris occurs in lesions of great diversity indicates that some condition common to all must be the cause of the symptoms. The fact that it appears only after the heart-muscle has been long exposed to excessive strain points to the cause being situated in the muscle. All the functions of the muscle-fibers save that of contractility can be shown to be intact in many cases that suffer from angina pectoris. The alternating action of the heart is a demonstrable sign of exhausted contractility, and its presence is always associated with symptoms that are included in the symptom-complex of angina pectoris. The same exciting cause—extra strain on the heart—may provoke both the angina pectoris and the alternating action, and both may disappear with removal of the cause. The inference to be drawn from the consideration of these facts is that the symptoms that are included in the term "angina pectoris" are so closely associated with an impairment of the function of contractility of the muscle-fibers of the heart that in all probability angina pectoris will be found to be an evidence of the impairment of the function of contractility. James Mackenzie (Brit. Med. Jour., Oct. 7, 1905).

The importance of arterial reflex having its origin in the abdomen has not been fully appreciated. While the active processes of digestion are going on, there is an influx of blood into the splanchnic area. This drainage into the abdominal vessels is balanced in the general circulation by a systemic arterial contraction, evidently a reflex phenomenon originating in the splanchnic system, passing to the vasomotor center in the medulla and then transmitted to the systemic arteries. The changes in the systemic arteries are a reduction in size and an apparent thickening of the arterial wall. The degree of these changes depends on the kind of meal which has been taken. In the big eater and the wine-drinker the arterial contraction is associated with a rise of blood-pressure and a true increase of arterial tension. This reflex varies in delicacy in different persons. It exists

in all. The author is convinced that there is a relation between this phenomenon and angina pectoris, and cites several instances in support of his contention. He shows that this hypersensitiveness of the vasomotor center, even in grave angina pectoris, can be reduced, controlled, or even removed by dietetic measures, with the result that the anginous seizures are removed or greatly modified. In cases where the arterial spasm is associated with great anatomic change, either in the myocardium or in the coronary vessels, absolute cure can hardly be looked for, but in all cases the symptoms of angina pectoris may be much ameliorated by conducting the treatment in accordance with what they indicate. Owing to the varying degree of intensity of the symptoms, the writer suggests that in classifying the cases the simplest distinction might be found in the terms angina pectoris major and angina pectoris minor, the former being confined to those cases in which there is believed to be permanent anatomic change in the heart or its vessels. W. Russell (Brit. Med. Jour., Feb. 10, 1906).

The pain of angina depends upon vascular distention in the mediastinum, which is the result of a more or less localized vasodilatation and of a more or less generalized peripheral vasoconstriction. It would seem that the angina is not due to the organic lesions any more than is asthma due to emphysema, or migraine to atheroma of cranial vessels. The connection between the organic lesions and angina should then be ascribed to the chronic peripheral vasoconstriction, which constitutes the earliest stages of many forms of chronic organic disease of the heart and vessels.

Preventive treatment resolves itself into the prevention of exaggerated peripheral vasoconstriction, continuous or recurrent. Purin-free diet, cutting down of the intake of carbohydrates, especially the saccharine carbohydrates, and the fats, is advocated. Francis Hare (Med. Rec., Oct. 20, 1906).

Angina results from an alteration in the working of the muscle-fibers in any part of the cardiovascular system, whereby painful afferent stimuli are excited. Cold, emotion, toxic agents interfering with the orderly action of the peripheral mechanism, increase the tension in the pump walls or in the larger central mains, causing strain, and a type of abnormal contraction enough to excite in the involuntary muscles painful afferent stimuli. Mackenzie suggests that there is rapid exhaustion of the function of **contractibility,** which is, after all, only the fatigue on which Allan Burns laid stress. In a disturbance of this Gaskellian function is to be sought the origin of the pain, whether in heart or arteries. In stretching, in disturbance of the wall tension at any point, and in a pain-producing resistance to this by the muscle elements lie the essence of the phenomena. In a man with arteriosclerosis and high pressure, and all the more likely if he has a local lesion, a syphilitic aortitis for example, disturbance, at any point, of the tension of the wall permits the stretching of its tissues. Spasm or narrowing of a coronary artery, or even of one branch, may so modify the action of a section of the heart that it works with disturbed tension, and there are stretching and strain sufficient to arouse painful sensations. Or the heart may be in the same state as the leg muscles of a man with intermittent claudication, working smoothly when quiet, but instantly an effort is made, or a wave of emotion touches the peripheral vessels, anything which heightens the pressure and disturbs the normal contraction brings on a crisis of pain. Osler (Lancet, Mar. 26, 1910).

The immediate, precipitating conditions of a paroxysm are not known, but they are supposed to be connected with disturbances of the vagus, or, perhaps, the sympathetic nerves. Nothnagel reported a series of cases under the title "angina pectoris vasomotoria" which seemed to be due to a pure neurosis. They followed exposure to cold, and were ushered in by spasm of the peripheral arterioles, which presumably

produced the cardiac disturbance because of the increased exertion demanded of the heart in order to propel the blood through narrowed channels.

Broadbent describes angina vasomotoria as a comparatively favorable class of cases of high arterial tension associated with general arteriosclerosis and a hypertrophied heart capable of powerful contraction. "The circulation in the coronary arteries may be sufficient for ordinary needs, but when the arterial tension is further raised by exertion or increase of peripheral resistance attacks of angina are induced."

From a neuralgia or a neurosis true angina pectoris differs in being frequently fatal, in attacking men ten times as often as women, and in being associated with organic changes in the neighboring structures, viz.: the heart and aorta.

Lesions of the cardiac plexus and the branches of the vagus have been found in repeated instances of angina pectoris, but that such lesions are invariably present and essential to the disorder has not yet been proved. "The cardiac nerves may be seriously implicated in aneurism, in mediastinal tumors, in adherent pericardium, and in the exudate of acute pericarditis, without causing the slightest pain" (Osler).

The late Sir Benjamin W. Richardson regarded angina pectoris as an actual disease analogous (as Trousseau held) to epilepsy, and due to a disturbance in the sympathetic nervous system.

> Angina pectoris is, in the main, an angiospastic disease, and it may easily be understood how a spasm of the arteries may extend through the circulatory system. In the case reported, that of a man aged 70 years, the symptoms of angiospasm in the extremities, such as cyanosis and pain, were replaced by a true gangrene of the upper limbs. The patient had suffered from anginal attacks for two years, during which he had suffered pain and numbness in his right arm and hand. The gangrenous process appeared very rapidly and continued for three months, after which it healed completely, not leaving any traces whatever. It was noted that during the days which followed an attack of angina the gangrenous areas looked worse, and the secretion had a more disagreeable odor and was more abundant. E. Salvini (La Riforma Medica, March 23, 1907).

Debove says that in tabetic angina pectoris there is no organic lesion of the heart or large vessels, and that the attack must be regarded as a visceral crisis. Dana refers cardiac crises in tabes to a degenerative irritation of the vagus. It should, however, be remembered that aortic disease is rather frequent in tabetic patients.

In regard to the causation of attacks of angina pectoris in the graver cases which are associated with serious structural disease of the heart and vessels, J. Burney Yeo states that in by far the greater number of deaths from organic disease of the heart all the various lesions may be present which have been found in fatal cases of angina and yet no true anginal attacks have ever been complained of. In his opinion there is some additional circumstance needed to account for the angina. The most serious forms of angina seem to have a complex causation. First, there must be a neurosal element; the nerves of the cardiac plexus suffer irritation, and an intense cardiac nerve-pain is excited; this acts as a shock to the motor nerves of the heart, and thus reacts on the heart-muscle, which, in fatal cases, is already on the verge of failure from organic causes; and, if there should be excited at the same time some reflex arterial spasm, the heart will have to

encounter an increased peripheral resistance as well. In such cases the rapidity of the fatal issue is no argument against the neuralgic nature of the angina. In certain conditions, especially in habitual high arterial tension, strain is apt to fall (when the aortic valves are competent) rather on the first part of the aorta than on the ventricular surface, and anginal attacks are more prone to occur in these cases, as this part of the aorta is in such close relation with the nerves of the cardiac plexus, rather than in those cases in which the strain is felt on the interior of the cardiac cavities.

The causation of the less grave and more remediable forms of angina is also, in many instances, complex. A cardiovascular system feeble and poorly nourished on account of anemia may be submitted to undue strain; or there may be some intoxication—such as that of tea, tobacco, alcohol, gout, or some intestinal toxin—irritating the cardiac and vasomotor nerves, increasing peripheral resistance, and so exciting anginal attacks, which may altogether pass away and be completely recovered from. Vasomotor spasm as a unique cause of attacks of angina must be set aside as inconsistent with extended clinical experience.

Cases of angina pectoris, both of the milder and graver forms, occur without any evidence of vasomotor spasm or of heightened arterial tension; and the conditions of heightened arterial tension, together with a feeble cardiac muscle, very commonly coexist, without any tendency whatever to the development of anginal attacks. The argument in favor of a vasomotor causation has been inferred from therapeutic experiment and the relief to the paroxysm which has attended the use of agents which cause arterial relaxation. But most, if not all, of these vasodilators are also anesthetics, and, as Balfour has pointed out, it is probably to their anodyne action on the sensory cardiac nerves that they owe their chief efficacy; Grainger Stewart also has pointed out that nitrite of amyl has a direct effect on nervous structures, and that it relieves other forms of neuralgia.

Certain fallacious conceptions of angina pectoris prevail. Thus, in true cardiovascular angina pectoris, peripheral arterial sclerosis, cardiac hypertrophy, and high blood-pressure are essential. This is by no means always the fact. Arterial change may be widespread and the coronaries sclerotic without hypertrophy of the heart or rise in blood-pressure. The sclerotic or atheromatous process may be quite limited, localized to the beginning of the aorta, and only encroaching a little on the coronaries, while the peripheral vessels may be normal. Especially in syphilitic cases are the conditions liable to be thus localized. In some of the most serious cases there may be no abnormal arterial pressure, indicating, perhaps, a weakened cardiac muscle. The finding of aneurism or lesion of the aortic valves does not exclude angina, but is rather in its favor. The attacks are not always few in number, and following exertion, and life is not necessarily cut off within a few months after the appearance of the disease. Patients may live a number of years with comparatively frequent attacks. While comparatively rare in women, the disease is by no means unknown, and serious mistakes may be made in diagnosis, especially in nervous and hysterical cases. The cardiopath is often a neuropath also. Pain is not always excessive. It may be mild or even lacking; its radiation is variable. Even in fatal cases there may be no constant pain. Unconsciousness, though unusual, is seen at times, and, while the patient usually is afraid to move, and will not lie down, there are exceptions to this rule. Eructations or vomiting during an attack do

not prove it to be a false angina and not organic or cardiovascular. While the disease is very grave, there is no certainty that death is imminent. The kidneys, as well as the heart, must be investigated as regards prognosis. J. B. Herrick (Jour. Amer. Med. Assoc., Oct. 22, 1910).

PROGNOSIS. — The underlying condition is apt to prove fatal eventually, and it may end life in the first paroxysm; but a careful regimen may prolong existence for years, and Flint, Bendel, and Labolbary have each reported cases of recovery.

The signs of danger during any particular attack are the subjective sense of impending death and the feebleness and irregularity of the pulse. The general prognosis is, of course, influenced by the stage which the organic circulatory changes have already reached.

The pseudoattacks are apt to be repeated oftener than are the genuine, but the prognosis is good, both as to life and as to the final disappearance of the trouble.

In common with all other observers, the writer finds that angina pectoris is more common in the male than in the female, in the ratio of 63 to 48. The youngest patient in his series of cases was 29 years old; the oldest, 76. The longest duration of the recurring syndrome was seventeen years; the shortest was found in three who died in the first attack.

Consideration of the various forms of angina pectoris shows the following: In coronary sclerosis there were 56 cases in all, *i.e.*, 29 cases without other appreciable changes in the heart and 27 with other changes. Evidences which Forchheimer considers as pointing to coronary sclerosis are the existence of angina pectoris and certain changes in the aorta or the aortic valves.

In the aorta we find as evidence of sclerosis some dilatation. Most frequently a soft aortic systolic bruit is detected, which sets in a little after systole, most commonly combined with an accentuation of the second aortic sound, especially characteristic when the blood-pressure is low. Over the aortic area are found systolic bruits, differing much in character, sometimes soft, sometimes harsh, but, as a rule, unlike those of aortic sclerosis due to other causes. Moreover, the second aortic sound is accentuated, which Forchheimer says is a fairly reliable differential sign between arteriosclerotic changes in the valve and in the ordinary form of aortic stenosis.

In 1 case of syphilitic endarteritis there existed angina pectoris of a very severe type, the physical evidence of a mitral lesion and of myocardiac insufficiency. In 27 cases which were developed on other diseases, the beforementioned signs were present. The coexisting diseases were chronic myocarditis in 12, mitral lesion in 6, aortic lesions in 4, obesity of the heart in 4, alcohol, diabetes, chronic nephritis, of each, 2; syphilis and cirrhosis of the liver, 1. Nearly all of these had evidence of arteriosclerosis.

In the cases of angina in which coronary sclerosis alone existed we find 3 dead in the first attack and 7 others dead. Of the latter, 2 died of diabetic complications, 1 of complicating pneumonia in the status anginosus, death being due to acute cardiac dilatation, 1 of a cerebral and another of a gastric hemorrhage. So that, in all, in only 6 cases could death be attributed to the coronary sclerosis. The duration of the disease in these cases varied from sixteen months to seventeen years, and all were males. In the 29 cases of coronary sclerosis there is but 1 female.

When the obstruction is due to thrombosis or embolism, the attack is usually fatal, either immediately or later on, as the result of changes in the myocardium. The attack is always immediately fatal when one coronary artery is closed. As a rule, death occurs instantaneously where the descending or circumflex branches are completely closed, but occasionally the patient survives for a few days, as is shown by myocardial infarcts found *post mortem*. Forchheimer's experience leads him to

believe that when both cardiac asthma and angina pectoris are present from the onset the outlook for improvement is very small. But he does not agree with Neubürger, who states that in coronary sclerosis there are 3 stages of myocardial changes, which develop and which are always fatal.

So far as the duration of the disease is concerned, aside from those who died in the first attack, in 8 the disease lasted from one to two years; in 4 from two to four years, and in 1 for seventeen years. Of those alive, 4 have had the disease from eight to ten years, the same number from five to eight years, and 10 from four to five years. F. Forchheimer (Jour. Amer. Med. Assoc., from Ill. Med. Jour., May, 1910).

TREATMENT.—During a paroxysm the first remedies to employ are such as will dilate the arterioles. **Nitrite of amyl** is the best because it acts with the greatest rapidity. A "pearl" of this drug may be crushed in a handkerchief or in cotton placed in the bottom of a glass tumbler, and inhaled. **Nitroglycerin** may be injected subcutaneously ($\frac{1}{100}$ to $\frac{1}{50}$ grain), or a tablet of this substance may be masticated, or a minim of **spiritus glycerylis nitratis** may be placed upon the tongue. It is readily absorbed from the mouth and acts almost as quickly as when given hypodermically. **Erythrol tetranitrate** has an action like nitroglycerin, but milder and decidedly more prolonged. It may be given in tablets of ½ to 2 grains.

Angina pectoris is due exclusively to a pain in the diseased aorta, and is always accompanied by a peculiar anguish. The lesions causing the pain are in the first part of the ascending aorta. The attack of pain is brought on by an emotion or an effort, and these causes are precisely those which increase the blood-pressure. The diseased aorta is not painful under ordinary conditions, but the pain develops as the blood-pressure rises, and it is favorably influenced by any measure that reduces arterial tension. Josué (Arch. des Mal. du Cœur, Oct. 1, 1908).

Erythrol tetranitrate has a less marked, but more lasting, effect than nitroglycerin. It is especially indicated in those patients who are awakened at night by the pains. Huchard and Fiessinger (Jour. des praticiens, Dec. 11, 1909).

The treatment of an actual attack of angina pectoris demands three considerations: (1) **Rest,** to promote restoration of heart-power; (2) **vasodilators, morphine,** to relieve the pain when this is not achieved by rest and amyl nitrite or nitroglycerin. In cases of severe spasmodic pain in middle-aged people, **amyl nitrite,** by lowering arterial tension, may provide instant relief; but in those cases of advanced fibroid degeneration in old people in which severe, prolonged, frequently occurring attacks of cardiac pain render life a burden, the only drug which seems to give relief is morphine. F. G. Thomson (Med. Press and Circular; Jour. Amer. Med. Assoc., Aug. 27, 1910).

The **nitrites** are sometimes marvelously efficacious in checking an attack, and their failure to give benefit does not exclude true angina. In some cases **digitalis** does more good than all the nitrites or iodides, and in this the writer's experience agrees with that of Romberg, who advised it in some cases. J. B. Herrick (Jour. Amer. Med. Assoc., Oct. 22, 1910).

Relief by these means is often immediate; but, if not, **ether** should be inhaled. **Chloroform** is also advised by excellent authorities. Flint thinks it not without danger, if the heart is weak; ether, on the other hand, is a stimulant. **Morphine,** subcutaneously, is a valuable and sometimes an indispensable remedy. Whittaker advised that it be given with caution in a condition which may anyway terminate in sudden death. The

morphine (¼ grain) may be guarded by **atropine** (1/150 grain), and in case of alarm also by **strychnine** (1/30 to 1/20 grain). **Electricity** has also been recommended.

The writer has never witnessed any fatality from **morphine**, but has always found it efficient in relieving the pain besides combating the spasm. **Nitrite of amyl** not only relieves but keeps the patient tranquil when he knows that he has it always with him. **Local heat** is also useful during an attack, and applications of dry cups in the axilla or on the back. When there is much dyspnea inhalation of **oxygen** is extremely beneficial. Michaelis (Therap. der Gegenwart, Dec., 1909).

Factors capable of bringing on the pain should be carefully avoided; every renewal of it keeps up the sum of stimuli. If for this end **absolute stillness in bed** be required, then bed it must be, with the corresponding **reduction of food.** If at first the attacks are not abolished, they will be mitigated, and will gradually taper off. All measures, medicinal, dietetic, etc., known to reduce arterial pressures should be enforced. Sir Lauder Brunton's potent means, the **nitrites,** are indispensable. To guard against vagus inhibition, **atropine** must be administered regularly. In very painful cases **morphine** may be needed also. An **ice-bag** applied cautiously and intermittently to the upper thoracic spine may prove helpful. The cause then requires treatment. Of new remedies two have seemed in the author's experience to be efficacious, more especially in angina minor—namely, (*a*) the **high-frequency current,** and (*b*) the administration of the **lactic acid bacillus** by the method of Metchnikoff. Baths and massage cannot be prescribed in any urgent stage of the disease. Causes of eccentric irritation must be discovered and neutralized. The patient must be warned never to swallow quickly, nor to bolt large morsels. **Diuretin** and **aspirin** have their advocates. **Chloroform** is very dangerous in angina. In syncopic failure of the heart **artificial respiration** should be tried. Allbutt (Brit. Med. Jour., Oct. 16, 1909).

Hot and stimulating applications over the precordia, such as a strong **mustard poultice,** are appropriate, as are also **heat** and **friction** for the extremities. Sometimes an **ice-bag** is put over the heart. By some it is preferred to heat. **Alcohol** and **aromatic spirit of ammonia** are of benefit in case the cardiac action is feeble. Syncope demands such drugs as **digitalin, caffeine, strychnine,** and **camphor,** employed hypodermically.

Angina pectoris with pseudostenocardia. The angina is due to probable endoaortitis, and is relieved by an exclusive **milk diet** and **theobromine** for two weeks. Then, one week every month, milk diet and **sodium iodide.** During the balance of the month, special diet, with the theobromine continued. H. Huchard (Jour. des Praticiens, Feb. 23, 1901).

The writer has employed various forms of **theobromine,** particularly **diuretin,** in a number of cases for several years, and finds it efficient in true angina pectoris. It is well borne in doses of 3 to 3.5 Gm. per day (45 to 52 grains). Occasionally it produces headache. Breuer (Münch. med. Woch., Phila. Med. Jour., Dec. 6, 1902).

Good results obtained from **theobromine** in angina pectoris. In 1 case a man of 46 had been suffering for two months from repeated attacks of angina pectoris, recurring so constantly that he did not dare to go to bed; the attacks only lasted a few minutes, but had already induced great debility and distress. Examination revealed insufficiency of the aortic valve. He was given 0.5 Gm. (7.5 grains) of theobromine, and the dose was repeated at bedtime. There were no further attacks then or later. The treatment with theobromine must be long kept up, for months and

years. It is effectual in other disturbances from arteriosclerosis as well. Two of the author's patients recently had vertigo and were afraid to venture into the street on foot, but have been free from the vertigo since they have commenced taking theobromine. Marchiafava (Policlinico, Feb. 28, 1909).

Prolonged rest in bed advocated in true organic cases. Marked improvement noted in most of the 20 cases studied. The patient should remain in bed at least two weeks, prolonged to six or eight weeks in cases that cannot walk without bringing on anginal pain. **Milk diet** to be imposed from the start; later **farinaceous foods** added. Drug medication by **theobromine, nitroglycerin,** and even **morphine** and **digitalin** also utilized. Greatest improvement in old patients and those losing weight during treatment; least, in cases with associated aortic insufficiency. Fiessinger (Bull. de l'Acad. de méd., Nov. 29, 1910).

The present writer has known **oxygen** to contribute to a favorable result in collapse due to chronic myocarditis with dilatation of the left ventricle, and it might be well for a subject of angina pectoris to keep some ready in his house.

The painful attacks incident to cardiac disease, such as angina pectoris, also paroxysms of tachycardia, can be mitigated by causing the patient to belch up wind from the stomach, owing to the fact that the heart and the stomach are both innervated by the pneumogastric nerve. **Eructation** is produced by the following procedure: The patient, seated, takes a small drink of water and holds it in his mouth. He then throws his head as far backward as possible and swallows the water. The posture is such as to stretch the esophagus and induce in the pharynx a sensation which causes eructation, provided the result is not voluntarily prevented by the patient. It is well to warn the person that an eructation is desired; otherwise, he may restrain it out of a sense of decency. Max Herz Semaine médicale, June 3, 1908).

Dyspeptic disturbances are responsible for or at least aggravate angina pectoris in many cases. Great benefit can be derived from **magnesium oxide** and **peroxide** to neutralize abnormal production of gases and the gastric juice, and promote bowel functioning. Regulation of the diet between attacks is of supreme importance. Chlapowski (Med. Klinik, June 5, 1910).

Between attacks it is of vital importance to avoid the predisposing and exciting causes. **Rest** and moderation are demanded, especially after meals. As for drugs, **nitroglycerin,** taken after meals in doses just short of causing headache, has a distinct inhibitory effect upon the paroxysms. In some instances it might be better to order it every three hours, as its influence is not long continued. **Nitrite of sodium** (2 to 5 grains) may replace nitroglycerin.

Laxatives and **eliminative treatment** by **alkalies** are often of great value.

The persistent use of **potassic iodide** is very effective. Ten or fifteen grains may be given thrice daily before meals in half a glassful of water; or twenty grains three times a day for twenty days, followed by **nitroglycerin** for ten days. The iodide is believed to dilate the arterioles and to promote arterial nutrition. Sée supposed that also by enlarging the caliber of the coronary arteries it invigorated the myocardium.

Arsenic and **phosphorus** in small doses also tend to avert the paroxysms. In case of fatty degeneration of the heart they would be contraindicated. **Barium chloride** in doses of $\frac{1}{10}$ to $\frac{1}{5}$ grain after meals is a good tonic for cardiac inefficiency, and often relieves cardiac pain.

Quinine and methylene blue have also been recommended.

The treatment by saline baths and by the Schott method of exercises has a most potent effect in improving the condition of the cardiac muscle and vessels, and appears to have a direct effect in making the attacks less numerous and severe, and even in causing them to cease during a period of months or years. The movements must be made with especial care and caution in these cases, and the resistance at the onset must be at a minimum. The artificial saline baths should contain from 1 to 3 per cent. of salt, and from ¼ to 1 per cent. of chloride of calcium, and should gradually be strengthened by the addition of carbonic acid.

Massage three times a week and persisted in for months may be of great benefit.

In most cases it is best to prohibit alcohol.

The cardiac tonics—sparteine, strophanthus, strychnine, valerian, and in suitable cases digitalis—are of the greatest utility.

The general tendency to anemia and defective oxygenation must never be lost sight of, and general tonics, including the use of oxygen gas, will be of excellent service.

Attacks of pseudoangina may be treated with asafetida, ammoniated tincture of valerian, or compound spirit of ether, and the outward employment of heat, friction, and rubefacients. Sometimes recourse must be had, however reluctantly, to morphine. The statement in clear and decided language of a favorable prognosis is of great benefit. Between attacks the underlying condition should be carefully sought and treated.

Case in which during the attacks the pulse rate rose to 120 and the pressure to 240, varying directly with the severity of the pain. Following the administration of amyl nitrite, the pressure sank to 150, coincident with the cessation of pain, but pressure rose and pain returned as the effects of the drug wore off. Morphine and chloroform produced similar effects. The nervous system being evidently at fault, as shown by the erethism of the vasoconstrictor mechanism, he was given bromides with good effect. This case presents the typical features of arterial constriction, more marked in cases of aortic valvular disease than in other forms of angina. In all forms of angina much more efficient results can be obtained by attention to the nervous system than by cardiac therapy, and bromides are ideal for such a purpose. MacKenzie (Heart, vol. ii, p. 265, 1911).

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ANGIOMATA.

See BLOOD-VESSELS, TUMORS OF.

ANGIONEUROTIC EDEMA.

See ASCITES AND EDEMA.

ANHALONIUM LEWINII

(Mescal Button).—The mescal button is obtained from a plant growing in the valley of the Rio Grande, in Mexico. The plant is of the family Cactaceæ. The tops of the plant when dried constitute the commercial Anhalonium Lewinii, first introduced by Lewin. The buttons or seeds are brownish in color, shaped like a top, and from 1 to 1½ inches in diameter. They are hard and can be pulverized in the mortar only with difficulty. In the mouth, however, under the action of the saliva, they swell and rapidly become soft, imparting a bitter, nauseous taste and causing a marked sensation of tingling in the fauces. Four alkaloids,—mescaline, anhalonine, anhalonidine, and lophophorine,—closely similar in their physiological effects, have been extracted from this species of anhalonium. From the related

plant **Anhalonium Williamsi** the alkaloid **pellotine** is derived.

PREPARATIONS AND DOSE.—The following preparations may be used: Tincture (10 per cent.); dose, 1 to 2 drams (4.0 to 8.0 c.c.). Fluidextract (100 per cent.); dose, 7½ to 15 minims (0.5 to 1.0 c.c.). Powder; dose, 7½ to 15 grains (0.5 to 1.0 Gm.). The tincture and fluidextract should be made according to the processes prescribed in the United States Pharmacopœia for such preparations.

PHYSIOLOGICAL ACTION.—Lewin found anhalonium to be an intensely poisonous drug. A few drops of the decoction used by him in the frog sufficed to produce almost instantly changes consisting chiefly in the appearance of shrinking of the body, so that the batrachian seemed to pass into a mummified condition. Simultaneously the animal raised itself upon its extremities and remained standing in this position like an ordinary quadruped, or crawled about. After fifteen minutes this spastic condition passed off and the frog rapidly returned to the normal state. When larger amounts were given death occurred in tetanic rigidity. The symptoms produced seemed closely allied to those of strychnine, Lewin noting that even after the spinal cord was severed peripheral irritation induced tetanus. In pigeons it was found that the drug produced convulsive vomiting in a few moments when injected hypodermically. The bird spread its wings, crouched down to the ground, and when disturbed exhibited muscular twitchings. Later the head was drawn sharply back, the mouth opened widely, and general convulsions appeared. When death occurred the heart was always found in diastole. In rabbits the symptoms resembled those of strychnine poisoning.

In the human subject anhalonium in large doses produces an effect in some ways closely resembling that of Indian hemp: visions ranging from flashes of color to beautiful landscapes and figures, illusions of time and space, etc. This and related plants are employed as intoxicants by certain Mexican Indians in connection with religious ceremonies. According to Prentiss and Morgan, color effects constitute the main feature of the drug's action on the brain. Consciousness remains unimpaired throughout its effects. Mitchell states that sometimes symptoms resembling the visual phenomena of ophthalmic migraine are experienced. The after-effects were also found by him to be markedly unpleasant, nausea and headache appearing which lasted for several hours. Heffter in 1898 carried out investigations on himself with the object of determining which of the active ingredients of mescal produced the visual hallucinations. An alcoholic extract of the buttons equivalent to 4½ drams was taken, and afterward a corresponding amount of each of the alkaloids. The symptoms produced both by the alcoholic extract and by mescaline (1½ grains) were colored visual hallucinations, slowing of the pulse, pupillary dilatations, loss of time relations, heaviness of the limbs, nausea, and headache. Anhalonine and anhalonidine in like amounts induced sleepiness without visual phenomena, while lophophorine (3/10 grain) caused occipital headache, facial redness and burning, and a temporary slowing of the pulse. Mescaline was thus shown to be the active constituent of anhalonium in respect of the visual phenomena.

According to Dixon, who carried out careful pharmacologic studies of anhalonium in frogs, cats, and rabbits and witnessed its effects in man, the chief effects of the drug in therapeutic doses appear to be: (1) Direct stimulation of the intracardiac ganglia; (2) initial slowing of the heart; (3) elevation of arterial tension; (4) direct stimulation of the brain centers and of the motor spinal centers, as shown by an increase in reflex excitability.

Full doses of anhalonium induce motor weakness and inco-ordination. In still larger doses difficulty of respiration appears. Lethal doses, Dixon found, produce complete paralysis, and death is caused by respiratory failure.

THERAPEUTIC USES.—Prentiss and Morgan employed anhalonium in various conditions dependent upon **excessive nervous irritability,** with considerable success. While not a hypnotic in itself, the drug in therapeutic doses (7 to 15 grains) often removed the cause of the **insomnia,** and thus conduced to natural sleep. It has been credited with beneficial effects, espe-

cially in **neuralgic headache, acute delirium, mania, melancholia** and **hypochondriasis, hysteria, irritative cough,** and **colic.** Anhalonium tincture in drop doses has been claimed to be useful as a sustainer of the heart action. But little knowledge of its clinical value in circulatory disorders has as yet, however, been obtained. According to Landry, the drug is a useful adjuvant to digitalis.

The taste of the liquid preparations of anhalonium is bitter and unpleasant, but can readily be disguised. Lewin recommended for this purpose the use of fluidextract of licorice and elixir of yerba santa (fluidextractum eriodictyi). The powdered drug may be administered in capsules or cachets.

The chief untoward action to be feared in the event of excessive dosage of this drug is respiratory depression. S.

ANHIDROSIS. See SWEAT GLANDS, DISEASES OF.

ANIDROSIS. See SWEAT GLANDS, DISEASES OF.

ANIMAL EXTRACTS, OR ORGANOTHERAPY.— In a recently published work Parhon and Goldstein, of Bucharest, state that "the importance of the internal secretions in physiology and pathology can today escape no one. In respect to pathology proper, we may say that there is no branch of medicine in which the problem of the internal secretions can pass unnoticed." That organotherapy has also earned for itself an enviable position can scarcely be denied, but here the scientific methods which pathology normally imposes have not been utilized to the same degree, and empiricism still prevails to a very large extent. Textbooks of therapeutics and practice still adhere to the convenient statements that an organic preparation "is useful," that "it is recommended," or "has proven valuable" in this or that disease; that is to say, without attempting to define its mode of action. The cause of this is not difficult to find: So many assumptions as to the actual functions of the organs used therapeutically have been vouchsafed on totally inadequate experimental evidence that textbook authors adopt none. The writer of the present article has taken another course. Rejecting all assumptions based on inadequate data, he has collected all experimental and clinical facts available, and employed these as the stones used in the elaboration of an edifice to reach each conclusion. Time has sanctioned this course. The conclusions he published in his "Internal Secretions" in 1903, vol. i, and 1907, vol. ii, and elsewhere, have steadily gained adherents, supported as they have been by an increasing number of confirmatory facts contributed independently by experimenters and clinicians. He feels it his duty, therefore, to adopt his own views as the foundation of the following summary of organotherapy, knowing, as he does, that they will best subserve the interests of the practitioner and of the sufferers under his care.

THYROID GLAND ORGANOTHERAPY.—In the latter part of the last century, King, of London, showed experimentally that the colloid substance of the thyroid gland passed directly into the lymphatics. Schiff, of the University of Geneva, reviving views in 1859 previously held by many, found that this organ played an important part in the economy, through some substance which it secreted, and that intraperitoneal transplantation of the healthy gland in a dog shortly after thyroidectomy had been performed prevented the cachexia strumipriva and violent nervous phenomena which follow this operation. Then followed,

in 1882, the labors of the brothers Reverdin, succeeded, in turn, one year later by those of Kocher, of Berne, demonstrating that, in man as well as in animals, the same phenomena occurred under identical circumstances.

The principal postoperative symptoms noted were: marked weakness and fatigue; a sensation of cold, pallor, hardness, and dryness; edematous swelling, thickening of the skin, and loss of hair, all with, as nervous phenomena: muscular stiffness and pains; tetany, sometimes attaining the violence of true tetanus, and even clonic convulsions. The brothers Reverdin termed this condition *postoperative myxedema,* while Kocher called it *cachexia strumipriva.*

The thyroid gland *per se* was subsequently found to be responsible only for the myxedematous symptoms, however. The two external parathyroids, discovered in 1880 by a Swedish physician, Sandström, and the two internal parathyroids, discovered by a French physician, Nicolas, of Nancy, in 1893, and independently by Kohn, of Prague, in 1895, were subsequently shown through the labors of Gley, Vassale and Generali, Moussous, Jeandelize, and others to be responsible for the nervous phenomena, tetany, etc. Briefly, removal of the thyroid alone arrested development and caused myxedema (cretinism in the young), while removal of the parathyroids alone was followed by tetany and early postoperative death.

The observation of Schiff, confirmed by other investigators, that grafting prevented the morbid effects of thyroidectomy as long as the grafts lived, led Murray and Ord to try the use of thyroid extract in myxedema. Not only was it found to counteract this disease by these clinicians and many others since, but thyroid gland, which includes parathyroid; but the latter alone, as will be shown under a special heading, also proved valuable therapeutically in other disorders.

How are these favorable phenomena brought about?

PHYSIOLOGICAL ACTION.— In a recently published work on therapeutics (1911), one of the contributors states that: "the manner in which the thyroid gland presides over the nutrition of the body is unknown. It is generally admitted that it furnishes an internal secretion, that this secretion is formed by the living cells of the vesicles, and that it is poured into the colloid material they contain. But our knowledge," remarks the author, "has not advanced much beyond this point." This naturally suggests a corresponding lack of knowledge concerning the physiological action of thyroid preparations and their use as remedies. But here, as elsewhere in the realm of science, the world has not stood still.

In truth, the last three decades have brought out facts which account not only for the nutritional phenomena witnessed under the influence of thyroid preparations, however administered, but also for autoprotective or immunizing functions of the first order.

ACTION ON METABOLISM.— Some physiologists hold that the thyroid and parathyroids, by means of an internal secretion, "exercise an important control over the processes of nutrition of the body," as Howell states; others contend that the purpose of these organs "is to neutralize or destroy toxic substances formed in the metabolism of the rest of the body." Others again assert that it increases metabolic activity, especially catabo-

lism. The one great factor which stays all progress in this connection is the persistent identification of these functions as separate entities, whereas they are in reality the manifestations of a single function. That such is the case is easily demonstrable: No one can deny that "the processes of nutrition of the body" represent a phase (that of anabolism) of the process of metabolism, nor can any one deny that catabolism, the other phase of metabolism, serves to "neutralize or destroy toxic substances" formed in the body at large—and to break down fats, as is well known. If, therefore, *the thyroid secretion serves to activate metabolism,* as first shown by two Italian scientists, Vassale and Generali, all the other processes mentioned are also influenced by the thyroid. That such is the case has now been conclusively shown.

[Chantemesse and Marie, Ballet and Enriques (cited by Popoff, Arch gén. de méd., Oct., 1899), Bourneville (Arch. de neurol., Sept., 1896), and Shattuck (Boston Med. and Surg. Jour., June 30, 1904), Lorand (Lancet, Nov. 9, 1907), and many other clinicians, including myself, have noted that thyroid preparations caused a rise of temperature of several degrees and that it took part in the febrile process. These observations were controlled by those of Stüve and Thiele and Nehring (Zeit. f. klin. Med., xxx, p. 41, 1896), that thyroid extract increases over 20 per cent. the oxygen intake and to nearly as great a degree the carbonic acid output. This is evidently produced by the active agent of the thyroid secretion, iodine, for this halogen itself increases oxidation as well. Thus, Rabuteau, Milanese, and Bouchard (C.-r. de la Soc. de Biol., pp. 227, 237, 1873), Henrijean, and Corin (Arch. de pharmacodyn., ii, 1896) have all noted an increase of nitrogen excretion. Wood ("Therapeutics," 13th ed., p. 499, 1906) and Cushny ("Pharmacology and Therapeutics, 4th ed., p. 514, 1906) state, in fact, that iodine can produce fever.

Removal of the thyroid, on the other hand, lowers oxidation. Albertoni and Tizzoni and Magnus Levy (Zeit. f. klin. Med., xxxiii, p. 269, 1897) found, for example, that this procedure decreased markedly the output of carbon dioxide, and that it caused hypothermia. The fall of temperature is gradual, according to Lorrain-Smith (Jour. of Physiol., xvi, p. 378, 1894), and most marked, according to Rouxeau (Arch. de physiol., xxix, p. 136, 1897), at the end of the operation. The proportion of red corpuscles is reduced, according to Moussu (C. r. de la Soc. de biol., p. 772, 1903). Reverdin observed in man that the hemoglobin was also diminished, while Horsley noted increased sensitiveness to cold. Albertoni and Tizzoni and Masoin found that the blood contained less oxygen than normally.

This applies as well to removal of the parathyroids, which was found by Jeandelize ("Insufficance thyroidienne et parathyroidienne," p. 45, 1903) also to lower the temperature. That the thyroid apparatus can itself raise the temperature, is shown by the febrile process and sense of heat with flushing observed in the sthenic stage of exophthalmic goiter and when the thyroid apparatus is still overactive. When thyroid extract is given to such cases, the exchanges may be increased to a surprising degree—77 per cent. in a case observed by Hirschlaff (Zeit. f. klin. Med., xxxvi, No. 3-4, S. 200, 1898-99). The disease may, in fact, be brought on by thyroid preparations, as noted by Notthaft (Centralbl. f. inn. Med., April 9, 1898) and other clinicians. C. E. DE M. S.]

The process through which general oxidation and metabolism are sustained by the thyroid was shown by myself, in 1903, to be partly due to excitation of the adrenals by the thyroid secretion contained in the blood. Starling has since (1906) termed "hormones" substances which thus act as stimuli to other organs, while Kraus and Friedenthal, Caro, Hoskins, and others have found (1908-1910) that thyroid extracts excited the adrenals. This indirect action I also found in 1907 to be supplemented by a direct action on the phosphorus of all tissue-cells (and par-

ticularly of their nuclei), the iodine found by Baumann to be the active agent, in organic combination, of the thyroid secretion (as well as of the parathyroids, as shown by Gley), rendering the phosphorus more susceptible to oxidation by the hemoglobin.

[Telford Smith (Lancet, Oct. 7, 1897) and other clinicians have observed that the use of thyroid preparations in young cretins was sometimes attended by softening of the bones and bending of the legs, notwithstanding marked general improvement. When it is recalled that five-sixths of the inorganic matter of bone consists of calcium phosphate, it becomes a question whether the thyroid extract does not interfere with the building up of this tissue. That such is the case is further suggested by the facts that iodine, the active constituent of the thyroid secretion, and its salts, as shown by Henrijean and Corin (*loc. cit.*), Handfield Jones (cited by Wood, *loc. cit.*), and others, cause excessive elimination of phosphates and phosphoric acid, and that thyroid preparations, according to Roos, Scholtz (Central. f. inn. Med., xvi, pp. 1041, 1069, 1895), Pouchet (Bull. gén. de thérap., Sept. 15, 1905), and others, act in the same way. "Emphasis must be laid," writes Chittenden (Trans. Congress Amer. Phys. and Surgs., iv, p. 93, 1897), "upon the apparent connection between the thyroid gland and phosphoric acid metabolism," giving as example "the increased excretion of P_2O_5 after feeding thyroids to normal animals, and the great decrease in the case of animals with the thyroids removed."

The untoward effects of large doses of thyroid preparations on the nervous system, owing to its wealth in phosphorus and fats as manifested by tremor, tachycardia, optic neuritis [Coppez (Arch. d'Ophtal., Dec., 1900)], etc., also bespeaks such an action; Cyon (Arch. de physiol., x, p. 618, 1898), in fact, found that injections of iodothyrin excited the depressor nerve directly to such a degree that the vascular pressure often declined to two-thirds of the normal.

A familiar action of the thyroid preparations is a rapid reduction of fat in obese subjects when full doses are administered. The presence in the fat-cell of a nucleus rich in phosphorus whose purpose is promptly to promote oxidation of the fat when the organism requires additional carbohydrates explains this action. Schöndorff (Arch. f. d. ges. Physiol., lxiii, p. 423, 1896; lxxii, p. 395, 1897), in fact, found that the reserve fats could be exhausted before the nitrogenous tissues were affected.

The mode of action of the thyroid active principle, iodine, is suggested by the presence of this halogen in all nuclei, as shown by Justus (Virchow's Archiv, clxxvi, S. 1, 1904) and others. This means that iodine is found wherever phosphorus is present, while, as shown above, it is most active where phosphorus is known to be most plentiful. Now, chemistry furnishes a clue to the manner in which all the phenomena I have enumerated are present: "If a fragment of phosphorus lying on a plate is sprinkled with iodine," writes Wilson ("Inorganic Chemistry," p. 284, 1897), "the substances unite, and heat enough is produced to kindle the phosphorus." Nitrogen, hydrogen, and chlorine are ubiquitous constituents of our tissues, and the vigorous explosives they form with phosphorus and the intense liberation of heat the reactions entail are familiar features of the laboratory. Roos (Münch. med. Woch., No. 47, p. 1157, 1896) found that in a dog in nitrogenous equilibrium, iodothyrin "caused at once a marked increase in the output of sodium, sodium chloride, and phosphoric oxide" (cited by Chittenden, *loc. cit.*, p. 89).

Still, as Chittenden states (*loc. cit.*, p. 99), "according to Baumann, doses of 1 mg. of iodothyrin which contain only 0.1 mg. of iodine will produce a decided effect upon a goiter after three or four applications, thus clearly indicating that it is not the iodine *per se* that is effective, but rather the iodine compound." This will recall the observations of Notkin and White and Davies, that the action of the adrenal secretion resembles that of an organized ferment, and my own, that the adrenal principle with which the iodine is combined endows it with the properties of a ferment. Hence, the term "thyroiodase" I have applied to the thyroparathyroid secretion. C. E. DE M. S.]

When in the light above, we administer desiccated thyroid, which combines the actions of the thyroid and parathyroids, corresponding effects are

produced: It renders the phosphorus of all tissues, and all free substances, such as bacteria, wastes, toxins, etc., containing phosphorus, more inflammable or sensitive to the action of the oxygen in the blood. As this applies particularly to nerves and nerve-centers (all of which are especially rich in phosphorus), the adrenal center, and, therefore, the adrenals themselves, are excited, and, the adrenal secretion being the agent which takes up the oxygen of the air to sustain the blood-oxygenizing power, the supply of oxygen is also increased. All the various phosphorus-laden substances are thus not only rendered more readily oxidizable by thyroid extract, but this remedy also provides indirectly the required oxygen. Hence also the familiar influence of thyroid preparations on obesity, their action being mainly exercised upon the nucleus rich in phosphorus which fat-cells contain.

The wonderful effects of thyroid extract in cretinism can also be readily accounted for: The *rise of temperature* is due to the increased oxidation brought about by the thyroid and adrenal oxidizing substances acting jointly; the *enhanced metabolism* is a normal result of the augmentation of general oxidization, while the *increased appetite* is due to the resulting greater demand for foodstuffs. The marked improvement in *general nutrition* and *strength* is a self-evident result of the assimilation of a greater proportion of food materials, and the *rapid growth* likewise. The *cerebrospinal system* is particularly influenced owing to its wealth in phosphorus; hence, the *development of intelligence*. All organs being the seat of active metabolic activity and nutrition, the intestinal, renal, cardiac, and cutaneous and hepatic functions are all enhanced. Even the hair grows bountifully not only in cretinism, but when its loss is due to general adynamia. It counteracts *premature senility* in all its phases by restoring to the organism the one constituent which sustains the functional efficiency of all its parts.

This, it must be emphasized, is the aggregate of effects obtained with *small* doses, at most, 2 grains of the desiccated thyroid (which represents 10 grains of the gland proper), three times a day. When larger doses are given another order of phenomena is awakened: those of excessive burning up, as it were, of the tissues. The inflammability of all phosphorus-laden elements being markedly enhanced while the quantity of oxidizing substance is as greatly increased, the tissue elements are broken down more rapidly than they are built up, beginning with the fats, and the patient becomes emaciated.

THE THYROPARATHYROID SECRETION AS OPSONIN.—One of the functions credited to the thyroid gland, we have seen, is "to neutralize or destroy toxic substances formed in the metabolism of the rest of the body" (Howell). This is justified by many established facts. Tetany, as shown by the brothers Reverdin, we have seen, follows thyroidectomy; it is now recognized that this is due to a general toxemia. As these phenomena were arrested by administering thyroid extract, or by grafting, as long as the physiological action of these remedial agents lasted, it became evident that the thyroid supplied the blood with some substance which in some way destroyed the spasmogenic poison, *i.e.*, that the thyroid product was an antitoxic substance. This is further sustained by the facts: 1, that the blood

of thyroidectomized animals proved more toxic than that of normal animals, and that it caused convulsions; 2, that the urine of thyroidectomized animals was also more toxic than that of normal animals; 3, that the transfusion of blood of the latter into thyroidectomized animals counteracted for a time the toxicity of both their blood and urine. These and other facts had shown that the thyroid gland—mainly owing to the parathyroid secretion it contains—is endowed with antitoxic, or, as they have been sometimes termed, "detoxicatory," functions.

Yes; it is evidently not only "toxic substances formed in the metabolism of the body" that the thyroparathyroid secretion proves antitoxic. Charrin, Lindemann, and others have found, for example, that animals succumbed more readily to infections after their thyroid had been removed; Roger and Garnier, Kashiwamura, and others found that histologically the thyroid showed evidences of marked activity, while Torri noted that this was accompanied by an increased production of their colloid substance. Hunt has shown that thyroid feeding renders white mice much less susceptible to poisoning by acetonitrile; Vincent, Frugoni and Grixoni, Léopold-Lévi and Rothschild, and others have observed that thyroid preparations combated effectively various infectious diseases, including erysipelas and septicemia. The thyroparathyroid thus showed itself antagonistic to bacterial toxins and certain other poisons, as well as to toxic waste products.

This action is accounted for by the fact, pointed out by myself in 1903 ("Internal Secretions," vol. i), that the thyroid secretion is one of the important agents *in general immunity*—none of the active factors or antibodies of which had been traced to their source. I found, however, that this action was indirect, *i.e.*, that the thyroid secretion or extracts, while a constituent of the blood's antitoxin, or alexin, increased the immunizing power of the latter by enhancing the functional activity of the adrenals. This stimulating influence on the adrenals has since been sustained by the investigations of Hoskins and others experimentally, while the participation of the thyroid in the immunizing process was, four years later, confirmed by the researches of L. Fassin, of the Bacteriological Institute of Liége.

> Experiments to ascertain the influence of the thyroid gland on immunity. The first series of experiments in a large number of animals (dogs and rabbits) showed that the subcutaneous injection of thyroid product (fluidextract of the fresh gland, the thyroidin of Burroughs, Wellcome & Co.) is rapidly followed by an increase of alexin in the serum, a substance discovered by Buchner, generally considered as playing an important rôle in the defense of the body. This increase becomes evident as early as ten minutes after the injection; it becomes accentuated after one hour, reaches its maximum in twenty-four hours; then the proportion of alexin in the blood recedes more or less rapidly until the normal is reached. The effects of one injection rarely last less than twenty-four hours or more than two or three days. The writer also found that the oral administration of thyroid brought about corresponding effects.
>
> To control these results as to their direct relationship with the thyroid, the writer performed complete thyroidectomy in 9 animals. One alone, however, survived the operation more than fifteen days, tetany occurring in all, thus showing that the parathyroids had been completely removed. In all the operated animals there occurred a marked diminution of the hemolytic and bactericidal alexin, though it never disappeared

altogether. As the diminution of alexin might possibly have been due to traumatism, the operative procedures were repeated in fresh animals, leaving the thyroid *in situ*. But neither the traumatism nor even removal of the spleen caused a reduction of alexin. Louise Fassin (C.-r. de la Soc. de Biol., vol. lxii, pp. 388, 467, 647, 1907).

Further researches on the nature of the process through which the thyroid secretion enhanced the autoprotective power of the blood and of the phagocytic activity of the migrating and stationary (endothelial) cells brought me in 1907 to the conclusion that the thyroid and parathyroid secretions, acting jointly, served to sensitize all phosphorus-laden cells, normal and pathological, and that this thyroparathyroid secretion and Wright's opsonin were "one and the same substance." Among the more direct facts which sustained this opinion were that, while substances capable, as are the opsonins, of sensitizing or enhancing the phagocytic activity of leucocytes had been found in the blood-plasma by Denys and Leclef, Bordet, and others, and Nolf had shown that they were secreted by the red corpuscles, my own observations brought out (1) that the composition of these sensitizing substances was similar to that of the thyroparathyroid secretion, *i.e.*, that they contained iodine, nucleoproteid, and globulin, and (2) that opsonins, which had been assimilated to Bordet's sensitizing substance by Savtchenko and others, were destroyed at the same temperature as the thyroparathyroid secretion, *i.e.*, at 60° to 65° C. Briefly, besides being endowed with other attributes in common, the sensitizing substances of Denys, Bordet, etc.; Wright's opsonins, and the thyroparathyroid secretion all proved to be plasmatic products of the red corpuscles, and to show similar chemical properties. Hence my conclusion that it was as opsonin that the thyroparathyroid secretion produced its main effects, and the recommendation that thyroparathyroid preparations be used in various infections, acute and chronic, to enhance the opsonic power of the blood. My position has been sustained by several investigators.

The writer reported the results of experimental and clinical observations which had led him to conclude that the opsonins of the tissue juices and exudates were, to a considerable extent, the product of the thyroid gland while simultaneously taking part in the maintenance of health through its influence on metabolism. He noted elevation of the opsonic index of the serum after injections of thyroid extract into rabbits. A rabbit treated with 1.5 c.c. of the extract at two days' interval gave three days after the injection an opsonic index = 2, 4, for example. Another, given the preceding day 1 c.c. of the extract, gave an index of = 3.0. These results, obtained in many animals, and other experiments led the writer also to ascribe the opsonizing action of thyroid extract to the thyroglobulin of Oswald, which is normally present in the thyroid gland. Stepanoff (C.-r. de la Soc. de Biol., vol. lxvi, p. 296, 1909).

The writer, having also advanced the opinion that the glands with internal secretion probably play an important rôle in the phenomena of immunity, undertook to verify this view experimentally, as had Stepanoff, at the Pasteur Institute. The first series of experiments aimed to ascertain the influence of hyperthyroidization on opsonic variations in the blood of guinea-pigs and rabbits, using mainly the bacilli of tuberculosis, diphtheria, the *Bacillus coli*, and the staphylococcus and streptococcus. A large dose of thyroid (1 Gm. per kilo) was given the first day, but this was reduced daily. In this series, which included 116 examina-

tions, the writer states that he always observed that the opsonic power of the blood-serum increased very clearly after thyroid opotherapy. It was, in fact, considerably more than doubled in all but one instance, the exception being that of an animal in which an emulsion of *Bacillus coli* only increased the opsonic power one-half.

Might the ingestion of any animal substance by herbivora not have given rise to the increase of opsonic activity? The administration of corresponding quantities of horse flesh to control failed to modify the latter in any way. The writer found, moreover, that the leucocytes of a normal animal when treated *in vitro* with the serum of an hyperthyroided animal showed a distinct increase of phagocytic activity.

The second series of experiments had for its purpose to ascertain the effects of removal of the thyroid on the opsonic properties of the blood. The serum obtained from 4 dogs at the time of the characteristic accidents caused by thyroidectomy showed in every instance a most evident diminution of opsonic power. The same experiments conducted in the rabbit gave rise to the same results, *i.e.,* he always found a marked decline of opsonic power in thyroidectomized animals. He noted, moreover, that, while traumatism, even a musculocutaneous wound, could cause in a certain measure a reduction of opsonic power, the latter rapidly returns to normal, while it maintains itself a very long time at the same level in thyroidectomized animals. S. Marbé (C.-r. de la Soc. de Biol., vol. lxiv, p. 1058, 1908).

On the whole (referring the reader for experimental details to my work on the internal secretions), the physiological action of thyroid preparations may be summarized as follows:—

1. They enhance oxidation by increasing the inflammability of the phosphorus, which all cells, particularly their nuclei, contain, and by enhancing the functional activity of the adrenals.

2. Their power to enhance the inflammability of cellular phosphorus extends to pathogenic elements, bacteria, their toxins or endotoxins, toxic wastes, etc. As such they act as opsonins, and render these pathogenic elements vulnerable to the immunizing action of the blood and its phagocytes.

THE ACTIVE PRINCIPLE OF THYROID.—The thyroid product is an "iodized globulin." As Notkin and also White and Davies hold, the action of the thyroid secretion resembles that of an organized ferment. This finds its explanation in the fact that the thyroidin, to which this applies, is mainly a ferment *plus* iodine. The identity of this ferment suggests itself when we consider Baumann's analyses of his thyroidin. Among other tests, for example, he found that it was practically insoluble in ether and chloroform; that it was not destroyed by digestive ferments, and that it stood a temperature of 100° C. These are the specific tests of the oxygen-laden adrenal product, my adrenoxidase. Again, I found that this substance gave the tests of the plasmatic oxidase; Lépinois also found that the thyroid secretion contained an oxidase which gave the blue reaction with tincture of guaiac. We have seen, moreover, that adrenoxidase is a globulin: Oswald termed his product "thyroglobulin" and described it as an "iodized globulin." Several other facts could be adduced to show that this constituent of thyroidin is adrenoxidase. This means that it is merely the albuminous portion of the hemoglobin which enters the thyroid and parathyroids in large quantities with their rich blood supply.

Another constituent of thyroidin may be regarded much in the same light: nucleoproteid. Sherrington, Mil-

roy and Malcolm, and others have found that the granulations of the most numerous leucocytes in the blood, the neutrophiles, are composed of nucleoproteid, while the observations of Bail, Stokes, and Wegefarth, Sangree, and others have as clearly shown that these granulations leave the periphery of the cell. Here, again, we find in the secretion a supposed intrinsic component which, in reality, is but a commonplace constituent of the blood.

This harmonizes with the familiar fact that in the absence of its iodine the thyroid product is inactive. It indicates, moreover, the true nature of the functions of the thyroid and parathyroids, to collect iodine (brought to them by certain leucocytes, as I have shown elsewhere) and combine it originally with the free or albuminous hemoglobin and nucleoproteid. As Oswald holds, therefore, the thyroid product is an "iodized globulin."

PREPARATIONS AND DOSE.—The implantation of a portion of the thyroid gland beneath the skin was soon superseded by the hypodermic method, but the latter presented another drawback, that of requiring the constant attendance of the physician. Besides this the preparations often produced suppuration. The gland itself, therefore, administered in the form of desiccated powder in tablets or capsules, is preferred by the majority of practitioners. This presents also the advantage of conforming to the U. S. Pharmacopœia (*thyroideum siccum.*)

The *average dose recommended in* the former *Pharmacopœia,* 4 grains (0.250 Gm.), which suggests from 3 to 5 grains, *was excessive,* each grain representing 5 grains of the gland proper. The present official dose is 1½ grains.

For reasons submitted in the foregoing pages, *small* doses, from ½ to 2 grains, given three times daily in the adult, enhance metabolism, while larger doses so stimulate catabolism that they cause undue breaking down of the fats and tissues.

If kept up too long, the blood elements themselves (hemolysis), and even the tissues (autolysis) proper, may be destroyed. Five- or even 4-grain doses are never indicated, even in the treatment of obesity.

By loading up the circulation with toxic wastes, these excessive doses may also give rise to tetanoid movements and even to true tetany.

An important feature in this connection, however, is that the unstandardized preparations of desiccated thyroid vary in strength to a considerable degree, and that a small dose of a weak preparation may prove practically inert in practice. Dried thyroids are now officially required to contain from 0.17 to 0.23 per cent. of combined iodine. An imported desiccated thyroid, that of Burroughs, Wellcome and Co., is also standardized, each grain (representing about 6 grains of the fresh gland) containing 0.05 grain of iodine in combination. This product is labelled as representing a given amount of the fresh gland. It is available in small tablets of ½, 1, 1½, 2½, and 5 grains.

There is also on the market an imported article termed *iodothyrin,* a milk-sugar triturate of the thyroid active principle, 1 Gm. of which represents 0.0003 Gm. of iodine. The dose for adults is given as 10 to 30 grs. (0.6 to 2 Gm.), and is available in tablet form, each containing 5 grains (0.33 Gm.) of iodothyrin. Its manufacturers claim that, besides possessing the advantage of definite strength, it is devoid of extraneous matter. It is not

regarded as efficacious as the desiccated gland. It is a convenient preparation for young children, however, owing to the fact that it occurs as a sweet, whitish powder.

When preparations of thyroid gland —which include parathyroid—cannot be obtained, a *glycerin extract* may be prepared by divesting a sheep's gland of fat, and macerating it in an equal quantity in weight of glycerin twenty-four hours. From 2 to 15 minims of the extract may be given daily according to age.

> The writers have studied in goats the therapeutic effect of the following substances: thyroid gland; iodothyrin; thyroglobulin; thyroproteid; the products of peptic and tryptic digestion of the thyroid gland, including primary and secondary albumoses and further cleavage products, obtained separately. They find that thyroid gland and thyroglobulin have a marked and rapidly beneficial action. Secondary albumoses derived from hydrolysis of the thyroid are also active, but apparently less so than the former substances. Thyroproteid, iodothyrin, and the less complex products of digestion of the thyroid were wholly inert. Their experiments offer no ground for the supposition that iodothyrin is the active constituent of the gland, or even that it is one of the active constituents. Pick and Pineles (Zeitsch. f. exper. Path. u. Therap., Bd. vii, S. 518, 1909).

UNTOWARD EFFECTS AND THEIR PREVENTION.—The dangers attending the use of thyroid preparations depend, to a degree, upon the manner in which the remedy is administered. Beneficial doses, by raising the activity of all metabolic processes, prove tonic, increase the appetite, the strength, and the oxidations, as shown by a slight rise in temperature. When, however, the dose is too large, a weak, rapid pulse and shortness of breath, vomiting, cardiac oppression, a feeling of tightness around the chest, vertigo, and coma may supervene. Excessive doses have also caused anorexia, diarrhea, malaise, lassitude, and pain in the extremities; headache, various eruptions, urticaria, transient and papular erythema and eczema, and, in some cases, nervous manifestations; neuralgia, delirium, convulsions, delirium of persecution, aphasia, monoplegia, etc. When dried powder or compressed tablets that are not fresh are used, symptoms of ptomaine poisoning may be added to those mentioned. Hence, the observations that these preparations are more likely to produce such effects during the warm weather.

The best guide is the pulse. Any considerable quickening or palpitation should lead us to discontinue the drug until the cardiac action is again normal. There are no dangers in the use of the drug, provided we begin with small doses, from ½ to 1 grain, and gradually increase, watching the pulse. It should never be given to a patient who cannot be closely watched.

In some cases, although no other untoward symptom appears, the patient loses flesh. This is apt to occur when 2 grains of the dried gland three times daily in the adult is exceeded.

Chronic poisoning, characterized by rapid pulse, emaciation, weakness of the limbs, general debility, and mydriasis have also been observed in individuals who had undertaken, without medical advice, to treat their corpulency, and who had, therefore, subjected themselves to excessive doses.

TREATMENT OF THYROID POISONING.—As a rule, cessation of the use of thyroid preparations arrests the untoward effects. When such is not the case, however, arsenic, as

shown by Mabille, antagonizes the toxic phenomena. Fowler's solution, from 3½ to 5 drops three times daily, suffices in most instances to arrest all morbid effects.

Mabille's observation that **arsenic** obviates the unpleasant symptom excited by thyroid preparations confirmed. In 5 cases of idiopathic goiter, in 1 case of obesity, and 1 of infantile myxedema, iodothyrin was given in progressive doses of from 3⅘ to 30 or 38½ grains daily. At the same time arsenic was given, either in pills or as Fowler's solution, in doses increasing proportionately to the iodothyrin of 1/64 to 1/10 or even ⅛ grain daily.

The observations of the writer fully confirmed Mabille's experience, for, though the 7 cases took respectively 231, 111, 86, 320, 108, 296, and 125 iodothyrin tabloids, containing nearly 4 grains each, beyond occasional increased frequency of the pulse no symptoms of thyroidism appeared, so that the course could be continued uninterruptedly. Arsenic, therefore, appears to suppress thyroidism with greater certainty than atropine does iodism, and it is now possible to give iodothyrin safely in doses and for a period capable of producing definite therapeutic effects. Ewald (Die Therapie der Gegenwart, Sept., 1899).

The writer has also observed that **arsenic** exerts a specific influence upon the activity of thyroid. Patients who took an arsenical and thyroid preparation synchronously never complained of any deleterious effects, while those who were treated with thyroid alone occasionally exhibited untoward symptoms. So pronounced was the modifying power of arsenic that in the course of time he never prescribed thyroid preparations without adding arsenic in some form. Heinrich Stern (Jour. Amer. Med. Assoc., Feb. 15, 1902).

The addition of a cardiac tonic, preferably **adonidin**, to thyroid is recommended whenever the latter preparation is to be used for any length of time. The following formula is employed:—

℞ *Sodium cacodylate* .... 1/200 gr.
Adonidin ..... 1/30 gr.
Thyroid gland (dry powder) ..... 1 gr.

For 1 compressed tablet. When fresh adonidin cannot be obtained (its price is exceedingly high), **caffeine** may be substituted in doses of 1/6 grain. Thyroid therapy will receive a new stimulus as soon as the medical profession appreciates the fact that the addition to the thyroid of proper amounts of arsenic and a cardiac remedy will render the medication more efficient and deprive it of all or nearly all its deleterious effects. Heinrich Stern (American Medicine, Jan., 1910).

THERAPEUTICS.—The many disorders in which thyroid preparations have been recommended ("nearly all the chronic and many of the acute troubles known to humanity," as one author remarks) have naturally inspired considerable mistrust as to their actual therapeutic value. Gradually, as the harmfulness of large doses asserted itself and the physiological rôle of the thyroparathyroid apparatus became unraveled, however, their indications became better defined. It may now be said that in sharp contrast with the empirical methods of the past thyroid preparations, when employed intelligently, are of great value in many disorders, both acute and chronic.

As far as the author can elicit from his own investigations in practice as to the use of the thyroid gland and its preparations, the latter has a far wider sphere and use than may be realized by the average practitioner. He has tried its use and derived a great deal more benefit than he could imagine in such conditions as **myxedema, obesity, cretinism, exophthalmic goiter,** one case of **acromegaly,** and various **skin affections.** Samuel Robbinovitz (N. Y. Med. Jour., Nov. 27, 1909).

In the light of the functions attributed to the thyroid secretion in the foregoing pages, it governs tissue metabolism by rendering all phosphorus-laden cells susceptible to oxidation. When, therefore, the thyroid principle is deficient in the body, both phases of metabolism—including, of course, that of carbohydrates—the building up and the breaking down of tissues, are correspondingly inhibited. The most exaggerated expressions of this condition are, as is well known, the syndromes known as myxedema and cretinism. The characteristic symptoms of these disorders exemplify clearly deficient metabolic activity and its consequences. In myxedema we have, among other symptoms, for example, the low temperature, 95.5° F. in some instances, both in the mouth and rectum; great sensitiveness to cold, reduction of the urea output—sometimes to 50 per cent. of the normal—cyanosis of the lips, ears, and extremities on exposure to slight cold, and many secondary results of deficient metabolic activity, anemia with marked pallor, general relaxation of the arteries, muscular weakness, mental torpor and vertigo, and the cutaneous anesthesia. In the cretin, we have, besides, all the phenomena of arrested development, both physical and mental, as shown by the dwarfed body and the idiocy.

Hypothyroidia, or Hypothyroidism.—This is a condition akin to the above, but much less marked, frequently met in practice. The thyroid apparatus supplies a part only of that required by the tissues, and the resulting phenomena recall closely some of those observed both in myxedema and cretinism: chilliness and subnormal temperature, coldness of the extremities and sensitiveness to cold; fatigue on slight exertion; constipation with tendency to tenesmus; frequent attacks of migraine, "sick headaches" with nausea, vomiting, etc., and other periodic manifestations of autointoxication—due to inadequate reduction of waste products and their retention in the blood. The skin taking part in the process of elimination, urticaria and eczema are frequently observed, while transitory edemas of the brow, around the eyes, and sometimes of the face, even in the absence of albuminuria or casts, point to renal fatigue. Enuresis is commonly observed in children of this type and may persist to adult age. The patient is subject to frequent catarrhal disorders of the respiratory passages, usually ascribed to colds, but due mainly to vascular and glandular relaxation. A tendency to early alopecia, including the eyebrows (especially the outer third), is also noticeable—a sign of deficient general nutrition which coincides with a marked proclivity to early senility.

In women the menstruation appears late, owing to retarded development, and there is a proclivity to metrorrhagia due to laxity of the muscular coats of the uterine arterioles, while pelvic disorders are apt to occur owing to deficient support of the uterus, lack of tone in its muscular elements. Leucorrhea is also frequent, owing to relaxation of the glandular elements of the whole genital tract. Such women conceive readily, but abortion is very frequent among them; if the fetus is carried to the normal period, they have little or no milk. Children born of such mothers make up the largest number, if not all, the cases of cretinism, rickets, harelip, cleft palate, and other malformations usually ascribed

to hereditary influence. We are dealing simply with deficiency of the iodine in organic combination which the thyroparathyroid glands supply to the organism to sustain their intrinsic metabolism, *i.e.*, their vital activity.

If the mother has at her disposal sufficient store of thyroid secretion, the child does well; but if there is **thyroid insufficiency,** and especially if to this fault be added tuberculosis, hereditary syphilis, alcoholism, inanition, saturnism, or diabetes, the child will show undoubted signs of these taints, and will probably be a myxedematous cretin, with signs of rickets and achondroplasia, and to this cause may be assigned such malformations as harelip, cleft palate, bony deformities, hypospadias, or undescended testicle. Should the maternal taint be but slight, the child will merely be very backward, which is a matter of small amount in boys, and if after a time righted by the thyroid equilibrium being established; but in girls menstruation is late in being established; uterine retroflexion is frequent; the chest is undeveloped.

The author has often seen women nearing 40 years of age who are fat and whose menstrual flow is excessive take thyroid extract in order to reduce their **obesity.** He has often seen the menstrual flow in these women become modified, their stoutness decrease, and the women find themselves pregnant, when they had for a long time given up all hope of ever being so again. He has often by means of thyroid extract brought to a successful end a **pregnancy** in women who have repeatedly miscarried. It is often noticed that in adults incontinence of the urine can be stopped by rest in bed. This comes about from the fact that, while resting in bed, the patient is subjecting his tissues to large doses of thyroid secretion. In the case of a pregnant woman the increase of

Adipositas (8 months old). Weighs 36 pounds. (*Sheffield.*)

thyroid secretion often becomes excessive during the pregnancy, and the woman suffers from the symptoms of excessive thyroid secretion. Hertoghe (Bull. de l'Acad. Royale de Méd. Belgique, April 27, 1907).

Thyroid insufficiency is the cause of many of the phenomena noted in young infants, such as a tendency to obesity, to transient edema, cold feet and hands, scanty and brittle hair, vasomotor disturbances, vomiting, somnolency, and slight resistance to infections. With artificial feeding, these signs become more pronounced, with eczema, urticaria, tardy dentition, etc. It seems evident that nurslings receive in mother's milk some of the products of the mother's thyroid functioning. The physiological hypothyroidism of the newborn may assume pathological proportions; any derangement in thyroid functioning on the part of the mother or wet-nurse may lead to severe symptoms of hypothyroidism in the infant. In several instances in the writer's experience infants became myxedematous when the mothers had goiter. In other cases, the healthy infants of healthy parents became myxedematous when they had a wet-nurse with goiter. All these children were cured with thyroid treatment and change of nurse. Experimental research with goats has confirmed the fact of transmission of thyroid secretion by the placenta and in the milk. Concetti (Annales de méd. et chir. infantiles, Aug. 15, 1909).

Adipositas. Same case, back view. (*Sheffield.*)

The rudimentary forms of **myxedema** or **hypothyroidism in children** are particularly liable to escape recognition, while thyroid treatment in time is almost a certain cure. In a case of this kind a boy of 6 had not grown in the last two years, but seemed otherwise normal, although not particularly bright. Under cautious thyroid treatment by the end of eighteen months he had grown 11 cm., nearly 4½ inches. In 2 other cases the myxedema developed after severe measles or mumps, with acute

thyroiditis in the latter case. The thyroid treatment ordered was soon abandoned by the family, and the child developed pronounced myxedema, but after two years it spontaneously subsided. In a fourth case the myxedema developed after a severe fall over a balustrade, the throat in front bleeding from the injury. Thyroid treatment promptly cured the child. "Pasty" children, fat, pale, and flabby, may be suffering from hypothyroidism and require thyroid treatment. Stoeltzner (Jahrbuch für Kinderheilkunde, Aug., 1910).

Diagnosis in the early stage of the malady must be very largely a matter of exclusion and experiment. The patient comes complaining of debility, lack of energy, is chilly, the skin is dry, so also the hair, ideation is slow, the temperature may be subnormal and associated with a slow pulse rate. His complaint is chiefly regarding his weakness and lack of energy. If **thyroid deficiency** be at the bottom of the patient's trouble the administration of thyroid tablets three times a day for a short period will produce marked and continuous improvement. W. B. Thistle (Can. Pract. and Rev., June, 1910).

Hypothyroidia, in so far as nutrition is concerned, may be defined, therefore, as that condition of the body in which, owing to deficient production of the thyroparathyroid secretion, cellular metabolism is slowed sufficiently to inhibit more or less all functions. Hence, the value of thyroid preparations in **infantile marasmus.**

In **infantile wasting** the writer gives thyroid in a diluted milk and cream mixture with sodium citrate, 1 or 2 grains to the ounce of milk. In a day or two cream is gradually added, ½ a teaspoonful to the feeding bottle. Out of 80 cases thus treated 72 were infants under 9 months and their history was simply one of wasting. The other 8 had a wasting supervening on some acute diseases; 63 cases did well; 5 cases presented syphilitic histories in which wasting was a marked symptom. Mercury was first given and later thyroid. Three immediately gained and eventually recovered. In older children the results have also been favorable, except when tuberculosis was present. In children under 9 months, the author began with ⅓ grain of dried thyroid once daily. Larger doses often seemed to induce a diarrhea. In the giving of thyroid it is advisable to test the stools frequently to see whether they are acid or alkaline. In case acidity is found the bicarbonate of soda may be given three times daily, and when the natural alkalinity of the stools is restored the thyroid will begin to exert its beneficial results. No grave symptoms followed the thyroid therapy. In 6 cases a punctiform rash appeared, confined in 2 cases to the front of the chest. It was evanescent and disappeared without treatment in the course of twelve to twenty-four hours. In only 1 case was it necessary to stop the thyroid (three days) in order to cause the rash to disappear. J. W. Simpson (Brit. Med. Jour., April 30, 1910).

The wide range of usefulness of thyroid extract as a regulator of metabolic processes is not sufficiently recognized by the profession. The writer has seen several **marasmic infants** transformed into normal, healthy babies under use of thyroid, and in these cases it was necessary to use it for only a short time, the gland seeming to have been stimulated to increased functional activity by the use of the extract.

Its administration to mothers who have not enough milk for their babies has, in the writer's practice, with one exception, been followed by an increase in the flow, making it possible to get along without artificial feeding where such feeding had been necessary with former children and would have been necessary in these cases, as shown by decreased flow whenever the thyroid was withheld. E. W. Demaree (Western Med. Rev., May, 1910).

In contrast with this condition, and exemplifying clearly what we are to expect from thyroid preparations, is the opposite condition, that of

Hyperthyroidia, or Hyperthyroidism.—The opinion of Möbius that exophthalmic goiter or Graves's disease is due to overactivity of the thyroid has steadily gained the confidence of the profession in recent years. But this imposes the necessity of establishing clearly the diagnosis of this disease, for there are many disorders that are due to thyroid overactivity, the so-called "larval" or "aberrant" types, the "formes frustes" of the French, or "pseudo-Graves's" disease, which should not be confounded at all with true exophthalmic goiter, since the active or erethic stage of the latter is aggravated by the use of thyroid preparations, while the "pseudoforms" are benefited by these agents. This does not, however, militate against the fact that exophthalmic goiter and all the above-mentioned subtypes are expressions of thyroid overactivity, or hyperthyroidism. In all we meet, more or less defined—in proportion with excess of thyroid secretion produced—the same group of phenomena, all of which can readily be explained by excessive tissue metabolism and its consequences.

> The early diagnosis of **hyperthyroidism** will be aided by discarding such terms as Parry's disease, Graves's disease, Basedow's disease, and exophthalmic goiter and substituting in discussion and in print the more natural term, hyperthyroidism, and by remembering (1) that so-called cardinal signs are usually late signs in the development of hyperthyroidism; (2) that in the beginning of hyperthyroidism its manifestations are apt to be monosymptomatic and during this period the symptomatology is characterized by inconstancy and variability; (3) that a change in the nervous and mental state is the ever-present symptom and sign of hyperthyroidism; that this is frequently the only complaint in the beginning, and that a more intensive study of the whole individual supposed to be suffering from so-called hysteria or neurasthenia will frequently disclose other symptoms and signs of hyperthyroidism, and (4) that the fundamental source of error in the recognition of hyperthyroidism is rather in not looking than in not knowing. W. W. Graves (Jour. Mo. State Med. Assoc., Sept., 1911).

As is the case, in other words, when excessive doses of thyroid preparations are administered, there occurs: a rise of temperature, a feeling of abnormal warmth; tachycardia due to excessive excitability of the heart muscle; pains, trembling owing to a similar condition of all muscles; sweating due to overactivity of the sweat glands; vomiting and diarrhea owing to abnormal irritability of their gastric and intestinal neuromuscular supply. Excessive metabolism involving the production of a surplus of wastes, the kidneys are overburdened and overactive, and the cutaneous emunctories likewise, the latter causing pruritus and a papular eruption, beginning, as a rule, over the scapulæ. As in Graves's disease, hyperthyroidism and excessive doses of thyroid may produce apparent protrusion of the eyeballs, the palpebral muscles being retracted owing to their abnormal contractility.

> Case of a woman who for fifteen years had had a slight **enlargement of the thyroid** which never gave inconvenience. Some one advised her to take thyroid extract, and she took daily 5-grain tablets for over three months. After some weeks' medication she began to notice trouble about the heart. When examined she had a pulse of 140. Notwithstanding this tachycardia, the heart sounds were perfectly normal, and there was no enlargement of the organ. She showed the characteristic fine tremor of Graves's disease.

The thyroid extract was at once discontinued, and a week later the pulse had dropped from 140 to 110 and the tremor was distinctly less. Eight days later the tremor had entirely disappeared, and the patient had no further trouble, though her pulse kept up to 100. G. J. Preston (Maryland Med. Jour., Dec. 10, 1898).

Thyroidism in an infant from administration of thyroid extract to the mother, a woman aged 34 who had exophthalmic goiter. On December 24th thyroid extract (two 5-grain tabloids daily) was administered to the mother. On January 1st the child had been sweating profusely for several nights It was looking ill and was sleepless. It had vomited every morning for three days. The extract was consequently stopped for five days. The child immediately improved, and on January 4th was quite well. On the 9th, thyroid extract was again given to the mother. The next day the child vomited, was again restless, did not look well, and sweated profusely, etc. The child was weaned and after this remained perfectly well. B. Bramwell (Lancet, March 18, 1899).

The administration of thyroid gland substance, or thyroid extract, is capable, if given in sufficient amount, of inducing a toxic state which in almost every essential is similar to Graves's disease. An artificial state of **hyperthyroidism** is thereby produced, which duplicates almost in full the morbid syndrome. Even the characteristic exophthalmic symptoms have been observed after thyroid feeding by Auld, Béclère, and others, and Edmunds was able to induce proptosis, widening of the palpebral fissure, and dilatation of the pupils in six monkeys by this means, even after excision of a portion of the cervical sympathetic. A. R. Elliott (Amer. Jour. Med. Sci., Sept., 1907).

There seem to be two distinct types of chronic intoxication from perverted thyroid functioning, one depending on the sympathetic system and the other on the vagus system. In exophthalmic goiter the two types may be combined; the vagus type predominates during the remissions and the sympathetic type predominates during the exacerbations. The sympathetic hyperthyroidism is the primary, the vagus type being more of a secondary, compensating process, but it may assume the preponderance in time. The morbid functioning of the thyroid which entails this modification in the tone of these antagonistic nerve systems may be the result of infectious or bacteriotoxic influences. There may be isolated patches in the thyroid in which the secretion is perverted, while the balance may be sound; this would explain the cases in which, after removal of part of the enlarged thyroid, severe acute symptoms of hyperthyroidism developed. Kostlivy (Mitt. a. d. Grenz. gebietend. Med. u. Chir., Bd. xxi, Nu. 4, 1910).

For several years the writer has been seeing cases of hyperemic thyroid, or thyroid hyperemia, and, upon consulting reference textbooks, found pediatric literature quite barren of comment on this affection. The condition arises at *puberty,* and all cases seen by the writer have been girls. The usual history is that the patient has grown rapidly, has been busy at school, has been observed to be nervous, and then the discovery is made that the collar worn is unduly tight. An examination reveals a swollen neck, and the patient is brought to the physician. The gland is found to be symmetrically enlarged, occasionally the right lobe slightly in excess; the gland is firm, but yielding; no bruit is felt or heard. There is usually a moderate simple anemia. There may or may not be a tachycardia. The patient is markedly nervous; there may be a slight tremor. In 2 cases seen there seemed to be a tendency to exophthalmos and the entire clinical picture was that of a mild exophthalmic goiter, yet recovery was prompt, there was no return of the disease, and the resemblance to Parry's disease was in the end only a simulation. This transient hyperthyroidism, which in adults may be seen at menstruation, during pregnancy, and in sexual excitement, is in reality more or less physiological and represents the

overresponse of the thyroid gland to the stimulation of altered nerve activity, and, in the cases above mentioned, to the special altered internal secretions manifest at puberty. Demme and other French internists describe this as "school goiter," and a variety occurring in warm weather and occasioned in part by the wearing of constricting collars, as "summer goiter" and "garrison goiter."

The course of thyroid hyperemia is short. With proper treatment the condition should disappear in a few weeks or months, and in some cases the subsidence of the disease appears to be spontaneous, having no relation to the treatment pursued.

The treatment is largely a matter of **hygiene.** A rest from school activities; life in the open air, preferably in the country; good nourishing food, a change in the drinking water, and an avoidance of nervous excitement are the prominent features of the treatment. The anemia should be corrected and nerve sedatives administered as required. Small doses of **arsenic** exert a retarding influence on the overactive gland. F. B. Cross (Long Island Med. Jour., Apr., 1910).

With the pathogenesis of these two syndromes clearly defined, the various disorders in which thyroid preparations are indicated suggest themselves, viz., those in which any of the signs of hypothyroidism are more or less discernible. The pathogenesis of hyperthyroidism being also apprehended, the limitations of thyroid treatment also appear: the doses utilized should be adjusted in each case to the degree of hypothyroidism that is present.

Case of cretinism. Result of four months' treatment. Growth, 4 inches. Intellect approaching normal. (*Moore.*)

Cretinism.—This condition represents the extreme type of hypothyroidism in the young. The value of thyroid gland is such in this distressing disorder that it may be regarded as a specific—the only agent, in fact, which influences it at all. The earlier it is used,

however, the better the results; hence, the importance of early signs of the disease, the most prominent of which are in infants (see article on "Cretinism"), enlargement of the tongue and of the thyroid, myxedematous swelling, arrest of growth, delay in learning to speak and walk, relative deficiency of intelligence, dryness and scaliness of the skin, scantiness of the eyebrows and eyelashes, puffiness of the lids, and facies of old age.

> The enlargement of the tongue and of the thyroid are the most positive signs of cretinism in the infant. The shape of the nose and the complexion are not characteristic at this early stage, and the myxedematous swellings are not observed until after the end of the first year. Early diagnosis of acquired cretinism is still more difficult. Backwardness in learning to walk and talk is the most reliable sign. In the endemic regions the parents are now being educated to watch for the early signs. Von Jauregg (Wien. klin. Woch., Jan. 10, 1906).

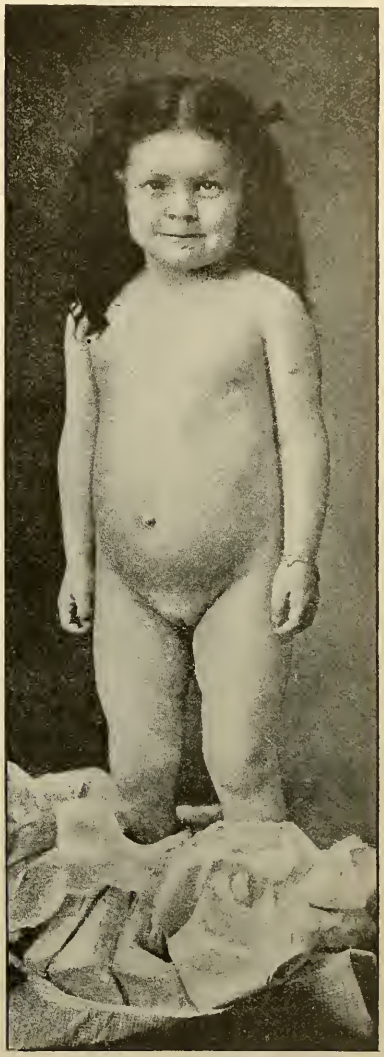
Soon, sometimes within a few days, the effects of whatever preparation is used begin to appear: the appetite increases, the temperature rises, and, nitrogenous foods being more perfectly assimilated, the nitrogen excretion rises —sometimes beyond that ingested. There is loss of weight owing to absorption and excretion of the excess of fluids in the tissues—an effect accompanied by marked thirst—in some cases, as observed by Marie, and increased activity of the kidneys. The red corpuscles and hemoglobin are simultaneously increased.

The wrinkles and edema disappear; the harsh, dry skin becomes soft, smooth, and moist; the hair from coarse and thin becomes thick and fine. Growth is resumed, and proceeds with great rapidity in children, sometimes at the rate of one inch per month. They do not, as a rule, however, grow tall. The brain responds more slowly, but considerable intelligence is gained in most instances, at times even that of an average child. The later in life cretinism develops, the better are the chances of improvement in this direction; occasionally none is observed. In other particulars, all degrees of cretinism, especially in sporadic cases, may be said to be improved, the best results being obtained in young children.

> Series of nearly 100 cases in which three years and more have passed since treatment was commenced. All degrees of **cretinism** and all ages were unmistakably benefited by the treatment, but the best results were obtained with the younger children. Complete cure was the rule in the milder cases, without serious impairment of the hearing, when treatment was begun in early infancy (at 6 weeks in 1 case). Von Jauregg (Wien. klin. Woch., Jan. 10, 1906).
>
> Since 1905, the Austrian government has been supplying thyroid tablets free of charge in seven endemic foci of **cretinism** with medical inspection twice a year. About 108,600 tablets were thus distributed in 1907, and 157,900 in 1908; the number of persons taking them was 1011, and 603 were still under the thyroid treatment at the close of 1908. The results are tabulated under various headings, special attention being paid to the increase in height as the most certain index of the benefit derived. Other findings are more liable to be influenced by subjective impressions. The report states that the results have been extremely satisfactory, confirming the efficacy of thyroid treatment as a prophylactic measure, especially in endemic foci of cretinism. In 677 cases followed to date marked improvement was obtained in 48.6 per cent., and only 8.6 per cent. showed no benefit from the course. The most striking proof of the beneficial influence of thyroid treatment on the growth is

the fact that in 377, that is, 85.7 per cent. of all cases, the former dwarf cretin children grew to be taller than the normal standard for their age. As a rule, treatment was restricted to

growing power of the preceding years had been held in reserve, until suddenly released by the thyroid treatment, when it made all its force felt in a relatively short period. A large number of the



Thyroid extract in cretinism. Cretinic idiot, 7 years old when thyroid treatment was begun. Had ceased to develop when 3 years old. Changes after one year's treatment. Growth 6½ inches. (*J. B. McGee:* Cleveland Medical Gazette, December, 1900.)

school children: the oldest cretin was 26 years old. Even after 20 a number of the cretins grew much taller and the other symptoms of cretinism became attenuated. This growth at this age is so surprising that it seems as if the more interesting cases are cited in detail. One cretin, 20 years old, grew 11 cm., but then refused to continue treatment, as he outgrew his clothes too fast He did not lose his milk teeth until after thyroid treatment was commenced,

although those of the second dentition were in place. A. von Kutschera (Wiener klin. Woch., June 3, 1909; Jour. Amer. Med. Assoc., July 17, 1909).

Case illustrating the far-reaching importance of the thyroid for the physical and mental growth and development and the lack of both with lack of thyroid functioning. The child was born with typical pure **myxedema** and at the age of 4 looked still like a 10 months' babe, being a pronounced **idiot.** No traces of the thyroid could be discovered on palpation. Thyroid treatment was then commenced, and in three months the child was transformed under its influence; it had grown 10 cm. in height, and has developed normally since, and is now lively and healthy. C. Doderlein (Norsk Mag. f. Laegevidenskaben, July, 1910).

To obtain such results, however, it is important to distinguish true cretins from idiotic dwarfs in whom thyroid is less beneficial or of no benefit whatever. These are the mongol or kalmuck idiots and the micromelic or achondroplasic dwarfs.

Mongol or *kalmuck idiots* resemble cretins in many particulars. The mouth is kept open by the protruding and thickened tongue; the hair is dry, scarce, and coarse; the palatal arches are narrow, the development of the teeth is delayed, constipation is the rule, umbilical hernia is frequent, etc. But their skin is less rough, and the general development is less retarded, though that of the brain, judging from the degree of idiocy, must differ but little from that of a cretin's. In this class of idiots the palpebral fissures are narrow and slope upward from the nose; the epicanthus projects markedly over the inner canthus, as is the case in most Chinese. Nystagmus, *i.e.,* oscillatory movements of the eyeballs, is also common. Thyroid treatment, though much less beneficial than in cretins, is, nevertheless, productive of good. The mental torpor is somewhat improved, the constipation and hernia are counteracted, and all functions seem to be activated.

Achondroplasic dwarfs are in reality but cases of fetal rickets, are normal as to intelligence, but their face is that of the cretin, the skin, especially about the hands, also recalling that of the latter. Other physical abnormalities are abnormal shortness and deformity of the limbs, marked narrowing of the palatal arch, and delay in the closure of the fontanelles. This condition, essentially due to morbid development of the bones and cartilages, is in no way influenced favorably by the use of thyroid preparations.

The *dose* should, of course, vary with the age of the patient from ¼ grain (0.015 Gm.) by the mouth in a 1-year-old child to 3 grains (0.2 Gm.) in the adult. As tolerance varies, especially in children, small doses should be used at the start and very gradually increased until not more than 1½ grains (0.1 Gm.) of desiccated thyroid in a child and 9 grains (0.6 Gm.) in an adult are given in divided doses daily. There is no condition in which the prevailing empirical method of administering remedies should be more rigidly guarded against than in this, since excessive doses of thyroid not only inhibit its beneficial effects by exciting violent catabolism, thus breaking down the tissues instead of building them up gradually, but they may, by doing so, cause death.

[What unfavorable results have been recorded can usually be ascribed to excessive doses. A certain critical author remarks, for instance, referring to personal experience of

this sort: "There was no longitudinal growth of the bones nor any poisoning to be observed, but great bodily prostration and an augmentation of mental apathy, together with emaciation dependent upon a loss of fat. From these unfavorable results of therapy it is seen that the view is untenable that athyreosis is the cause of cretinism. These observations are the reverse of the favorable ones made on the treatment of myxedema by thyroid gland, both in the young and in adults." The great bodily prostration, emaciation, increase of apathy, etc., speak for themselves. They had been caused by the excessive doses the critic had administered. C. E. DE M. S.]

The doses in which thyroid extract is usually prescribed are many times too large. The ordinary dose is officially quoted as from 3 to 10 grains. There are very few people, except certain types of lunatics, who will tolerate such doses under any circumstances, and not even they are able to do so unless this dose is arrived at by a gradual increase from small beginnings. It is a clinical fact, well recognized by those who have any real experience in the use of the drug, that, the more the patient requires thyroid extract, the smaller should be the initial dose. Since the writer has been using it he has been driven back and back in his doses. He now seldom begins with more than ¼ grain three times a day. He never prescribes a larger dose than 5 grains thrice daily, and then only in pronounced myxedema after several weeks' treatment. He has had many patients who were unable to take more than 1/20 grain once a day, but this was in each case quite sufficient completely to protect them from the symptoms of which they originally complained. In connection with the allotrophic disease, he suggests that the prophylactic dose for an adult should not exceed 1/10 grain three times daily, and that ¼ grain three times daily is quite a sufficient therapeutic dose to start with. Leonard Williams (Practitioner, Nov., 1911).

The *danger signals* are those of hyperthyroidism, previously described, the principal of which are an increase of temperature beyond normal, tachycardia, digestive disturbances, dyspnea, and tremor. When any of these phenomena appear, the dose should be reduced until the temperature becomes normal—which may be one or two degrees F. above the hypothermia usually observed in these cases. It should be remembered, however, that excessive doses may also cause hypothermia by inducing collapse. If the morbid effects continue, the use of the remedy should be stopped a few days and then resumed with a smaller dose. Should the hyperthyroidism persist notwithstanding, **Fowler's solution** in small doses soon arrests it. A common untoward effect is bending of the bones of the legs, owing to softening of the bones. The child should not be allowed to go about too much, or when bowing of the legs appears it should be placed in bed, as advised by Telford Smith.

[This is explained, from my viewpoint, by the action of the thyroid principle upon the phosphorus contained in the calcium phosphate, which plays so important a rôle in giving bone its solidity and rigidity. This suggests the use of calcium phosphate as an adjuvant to the thyroid to compensate for its loss. The influence of the thyroid secretion upon calcium metabolism has been well shown by the researches of Parhon, Macallum, and others. C. E. DE M. S.]

Case of **tetany** following an accidental overdose of thyroid extract in a girl aged 3 years who presented stigmata of cretinism. She was fat and plump, with reddish, somewhat cyanotic cheeks and abundant coarse hair. The anterior fontanelle was not closed. The hands and feet were cold and blue. The eyebrows were scanty. The abdomen was protuberant, but there was no umbilical

hernia. There was marked lordosis, and the tibiæ were curved. She was short in stature, and unable to say more than two or three words. Mentally, as well as physically, she was deficient and backward. The rectal temperature was 95°. Thyroid extract, 1 grain *t. i. d.*, was given, and the dose was gradually increased to 2½ grains *t. i. d.* All went well for a month, during which time she became more active and very mischievous. One morning she secured the box containing 5 tablets, each of 5 grains of the extract, and swallowed the whole. She "cried and screamed" a great deal that day. Six hours after she became "stiff and convulsed." A dose of castor oil was given, and later some bromide. There was no diarrhea. The writer saw her the next day; she was stiff, and presented pronounced signs of tetany. The eyes and limbs "twitched" a good deal. The face was very red. The characteristic "accoucheur hand" and arched feet were typical. The fingers and wrists were swollen, and moving the joints made the child cry. The whole of each limb and the back were stiff and painful. The deep reflexes were increased. The pulse was very quick, and the child was feverish. She was unable to stand or sit without support.

The treatment was suspended for a fortnight, and the symptoms gradually disappeared. Then ¼ grain of thyroid extract was given *t. i. d.*, increased to ⅓ grain. During the week after resuming the drug the "accoucheur hand" was again noticed. The dose was again reduced, but later increased. One month later a slight recurrence of the "accoucheur hand" compelled reduction of the dose of thyroid. Subsequently, though on continuous treatment, no recurrence of the tetany has been observed. G. W. R. Skene (Med. Review; Antiseptic, May, 1911).

[In the above case the toxic dose of thyroid produced excessive catabolism and an accumulation of waste products in the blood. Hence, the tetany which is also produced when deficiency of thyroid also leads to accumulation of spasmogenic wastes because the latter are not submitted rapidly enough to hydrolysis, a process for which the thyroid secretion prepares the wastes by sensitizing them. C. E. DE M. S.]

An important feature of the thyroid treatment of cretinism is the necessity in practically all cases of continuing it to prevent recurrence. The only permanent benefit when thyroid is discontinued is the skeletal growth, though the original morbid phenomena never return with the same intensity.

Several cretins occasionally occur in the same family, from the same mother, long intervals between births indicating the permanence of the pathogenic influence in the parent. Herman H. Sanderson (Jour. of the Mich. State Med. Soc., April, 1906), for example, observed 3 cases in one family, the patients being 21, 11, and 8 years of age, respectively. This points to the need of administering thyroid to the mother after the birth of a cretin, and during any subsequent pregnancy.

Studies and experiments in the regions in which hypothyroidism and athyroidism, which are known to cause **idiocy**, prevail—several mountainous districts in the Alps and the Karst Mountains with clay and lime subsoil. With the writer's research as a basis for work, local physicians were instructed to administer thyroid tablets to certain idiots and to report on the results; 124 persons were thus placed under observation. In 80 per cent. a marked improvement was obtained in four to eleven months, under administration of quantities of 36 to 100 Gm. (1 to 3 ounces) of thyroid substance; 12 per cent. showed no improvement within one year, while 8 per cent. did not tolerate even small doses well. In nearly all cases the integument became fairly normal, the height increased a little, and the intellectual qualities improved. Wagner (Jour. Amer. Med. Assoc., Feb. 6, 1909).

Myxedema.—Thyroid preparations are no less efficacious in this disease, which typifies hypothyroidism, in the adult than in cretinism, of which, in fact, this disorder is the prototype in adults. Here, again, we obtain those striking changes which clearly indicate that the remedy replaces in the organism a constituent necessary to the vital process itself, and the least deficiency of which impairs all functions. This is further shown by the necessity of administering it continuously, year in and year out, as in cretinism, to prevent recurrence.

Under the influence of thyroid preparations the morbid symptoms disappear. The dense, swollen tissues rapidly recede, causing loss of weight; the projecting abdomen resumes its normal contour; the skin loses its roughness and dryness; the hair grows more or less abundantly; the face loses its coarse and expressionless appearance, the wax-yellow color of the skin being replaced by a normal hue; the cyanosis of the lips, ears, and nose disappears. Even the slow and monotonous speech and mental torpor are promptly done away with, and if the case happens in an adolescent stunted by the disease growth is resumed and progresses rapidly, as in cretinism. The physiological action is precisely that defined under the preceding reading, since we again meet with a rise of temperature and all the phenomena that denote increased metabolic activity, including a marked increase in the urea excretion. Menstruation, frequently suspended during the disease, soon returns. The appetite markedly increases, and the patient experiences a feeling of well-being.

The *dose* generally employed in this disease is, as a rule, too large; 1 grain (0.065 Gm.) of desiccated extract daily, gradually increased until 2 grains (0.12 Gm.) are given three times a day. Even smaller doses have brought about favorable results.

> Case of **myxedema** in a woman of 60. Entire recovery of the patient was obtained under thyroid treatment on the principle of gradually increasing doses, commencing with doses so small as to have actually no action or next to none. For two months the daily dose was only 0.5 cg. (¾ grain), and then 1 cg. (1½ grains) was taken and continued every day. By the end of six months the patient was as well as before the onset of the myxedema, and has kept well during the year since, still continuing her daily dose of 1 cg. of the extract, representing only about one-thirtieth of a lamb's thyroid gland. Alsted (Hospitalstidende, xlvii, No. 50, 1904).

Inasmuch as myxedematous patients are, as a rule, more susceptible to thyroid preparations than normal subjects, it is always best to begin with small doses, since the degree of activity of the patient's own thyroid, though greatly reduced, is an unknown quantity. The presence of unexpected activity is the main underlying cause of the so-called "susceptibility" often met with, a very small dose of the desiccated thyroid sufficing in such patients to raise the standard of thyroid activity to its normal level. Again, as I have shown elsewhere (see "Internal Secretions," 1st ed., p. 1139, 1907), there is a true cumulative action of the thyroid secretion (thyroiodase) when thyroid preparations are administered, and there comes a time when toxic phenomena appear, even under the influence of very small doses. The temperature is the best guide. As it is below normal in all cases, the doses should be regulated in such a manner as to raise it to normal, reducing them

as 98.6° F. (37° C.) is exceeded. The quantity required—usually somewhat larger in winter than in summer—by each patient may thus be readily determined while avoiding cumulative effects.

In some cases it is well to ascertain whether a low blood-pressure is not perpetuating the peripheral hypothermia by causing the blood to recede to the deeper great trunks. This may be done by giving strychnine simultaneously in doses of $\frac{1}{40}$ grain (0.0016 Gm.) three times daily. By stimulating the vasomotor center, it causes the vessels to contract, and thus to project the circulating arterial blood into the peripheral capillaries. Strychnine, moreover, as shown by I. N. Love, tends to prevent the untoward effects of thyroid preparations.

An important feature of the thyroid treatment of myxedema is that the patients should be kept in bed the first few weeks and not allowed to get up suddenly, to avoid sudden syncope—the cause of death in several cases on record. This precaution is especially necessary in aged and weak patients and quite as much where the improvement is rapid as in less favorable cases. As emphasized by Combe, Seymour Taylor, and others, alcohol should not be used during the treatment.

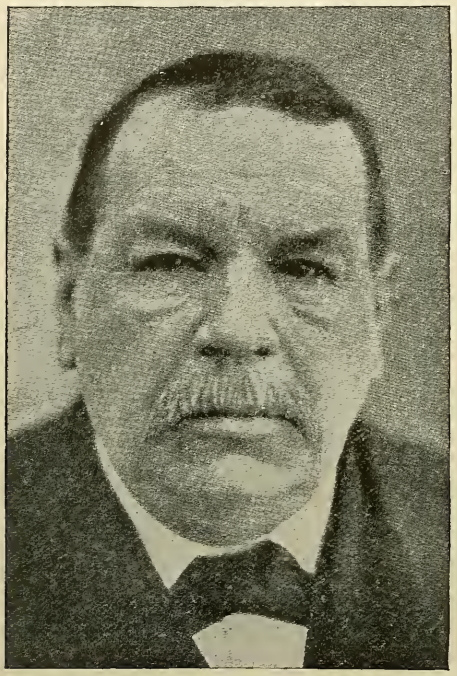


Fig. 1.—True myxedema. (*Hertoghe:* Bulletin de l'Académie Royale de Médecine de Belgique.)

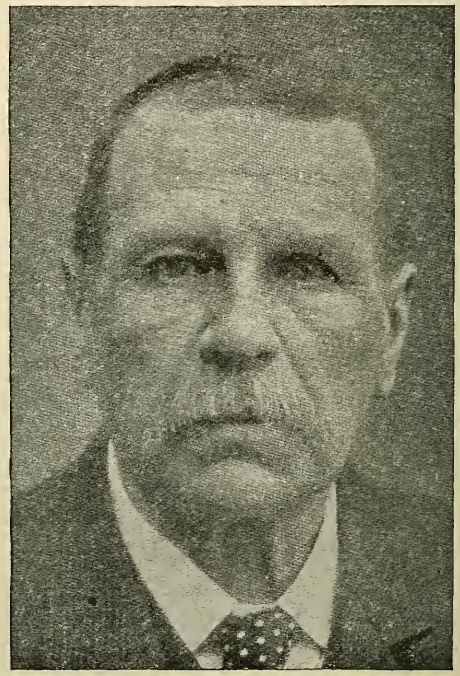


Fig. 2.—The same patient after thyroid treatment. (*Hertoghe:* Bulletin de l'Académie Royale de Médecine de Belgique.)

Bourneville, Lancereaux, and other clinicians have called attention to the fact that symptoms of myxedema do not appear in infants until they are weaned. This is because the mother supplies her suckling what thyroid secretion it needs to satisfy the needs of its cellular metabolism. Thyroid administered to a nursing mother is also transferred to the nursling in such a

degree, in fact, that the latter may present toxic phenomena. This suggests additional caution when the remedy is used in myxedematous women during pregnancy and lactation.

Contraindications.—When any adynamic cardiac disorder is present, the initial dose should be very small and very gradually increased, giving digitalis simultaneously if indicated by the cardiac trouble. When **angina pectoris** accompanies myxedema, small doses are beneficial, especially if the patient is placed on a vegetable diet.

Occasionally aged subjects fail to respond to the thyroid treatment alone, and the disease progresses until mental aberration, melancholia, or even maniacal disorders supervene. The depressed forms of mental disorder are probably due to the low blood-pressure which characterizes the disease, and which the thyroid tends to increase. Strychnine counteracts this untoward action, however, while enhancing the beneficial effects of the thyroid preparation.

> Case of a man of 42 years, treated with thyroid gland. Speedy improvement occurred, and in a few weeks all the symptoms disappeared, the weight diminishing from 13 to 10 stone. For several years he has taken thyroid gland regularly, and has thereby maintained a nearly normal standard of health. Straitened circumstances then prevented him from buying thyroid glands. A fortnight after their deprivation several of the original symptoms returned, and in less than two weeks thereafter nearly a complete picture of **myxedema** was reproduced, with, however, scarcely so advanced a development of the symptoms as in the original state. Thomas Fraser (Brit. Med. Jour., March 3, 1906).

The *danger signals* when thyroid is used in myxedema are, as in cretinism: tachycardia, palpitations, prostration with sweating, rapid emaciation, gastrointestinal disorders, anemia, headache, and in some cases excitement recalling hysteria. When the doses (even though small) are too large for the patient, urticaria may appear. This is due to cutaneous irritation caused by the more or less toxic wastes produced

Fig. 3.—True myxedema; sister of patient in Figs. 1 and 2. (*Hertoghe:* Bulletin de l'Académie Royale de Médecine de Belgique.)

in excess owing to the excessive catabolism induced, and which the kidneys cannot eliminate with sufficient rapidity. Cessation of the drug for a few days usually causes all these morbid effects to disappear, after which the remedy may be resumed in very small doses.

> Case illustrating in turn excessive and deficient activity of the thyroid in a child of 10 years: I. **Hyperthyroidism,** or exophthalmic goiter, with the classical symptoms of (*a*) exoph-

thalmos, (*b*) enlargement of the thyroid gland, (*c*) hyperexcitability, (*d*) a moderately rapid pulse, and (*e*) loss of weight. II. **Hypothyroidism,** myxedema, with the symptoms of (*a*) mental and physical dullness, (*b*) rapid increase of adipose tissue in irregular masses, and (*c*) pallor. III. Stage of balance, a disappearance of the myxedematous characteristics even though the weight was increasing. That other glands besides the thyroid were involved was probably true. This case illustrated the fact that many minor disturbances of the thyroid gland were probably unrecognized. S. V. Haas (Med. Record, Oct. 7, 1911).

After recovery, the patient's health can usually be maintained, *i.e.,* recurrence of the disease prevented, by administering small doses, 1 grain (0.065 Gm.) daily or every other day—just enough to sustain the temperature up to normal. In winter it is sometimes necessary to increase the dose somewhat to obtain this result. The prolonged use of the remedy does not, with rare exceptions, diminish the need of it to ward off the disease; cessation after several years' use will be followed by prompt recurrence of the morbid phenomena.

Case in a man of 36 years in which, after recovery from the initial treatment by the thyroid extract (which lasted two months in continuous dosage), the patient was never under treatment longer than four weeks at one time. The longest respite from thyroid therapy was for a period extending from May, 1907, to October of the same year, a period of five months; at the end of this time some of the old symptoms were again in evidence, namely, characteristic color, loss of expression, swelling and puffiness under the eyes; the mentality, however, continued good. The patient himself wanted to be placed under treatment again. An interesting feature of the case, aside from its rarity in these parts, is that if the patient takes more than three tablets a day, now that a cure is established, or continues the treatment for more than three weeks, he soon shows the symptoms of exophthalmic goiter, namely, nervousness, sleeplessness, slight exophthalmos, nausea, sometimes vomiting and general weakness. S. E. Simmons (Jour. Amer. Med. Assoc., May 15, 1909).

Occasionally a case is met with in which the thyroid treatment is followed by permanent recovery. Such cases are probably instances of temporary myxedema due to obstruction of the lymphatics through which the secretion gains access to the general circulation, or to some other factor interfering temporarily with the functions of the gland.

Between the cases in which continuous after-treatment is required and those that proceed to recovery are some in which respites of several weeks in the after-treatment are required to obtain the best results. This is a result obtained, however, only when large doses of thyroid are used in the after-treatment. There is danger in such cases of causing hyperthyroidism, *i.e.,* the symptoms of exophthalmic goiter, and it is preferable to reduce the dose until the exact quantity required continuously to keep the patient well is ascertained.

Thyroid grafting has been performed successfully in animals, especially by Christiani, and more recently in human subjects suffering from **myxedema** or **cretinism.** In the earlier operations, the improvement lasted only as long as the secretion that happened to be in the implanted tissues lasted, but in recent years better results have been obtained, the grafted fragments of thyroid assuming physiological functions

to a sufficient degree to prevent recurrence of the disease.

Case of a young woman who, becoming tired of the preventive treatment by thyroid, requested a substitute. The writers inserted portions of a sheep's thyroid gland in a series of grafts under her skin on two occasions three and a half months apart. The thyroid feeding was gradually diminished until it was reduced to a few drops a day of a liquid extract. About six months after the second transplantation the patient was delivered at term of a well-developed healthy infant. It was observed that during the latter months of her pregnancy the grafts became enlarged, evidently from congestion, being affected like the normal thyroid by the pregnancy. The successful termination of the pregnancy was ascribed in great part to the thyroid treatment, and especially the implantation of the functionally active thyroid under the skin. Lannelongue, in a case of a myxedematous infant, had previously implanted the first fragment of a sheep's thyroid in the human subject. The child's condition appeared improved, and the development of the disease became a little less active. Charrin and Christiani (Le Bull. médicale, July 11, 1906).

The writer has been experimenting on rabbits, the results encouraging further attempts to supply the missing function by implantation of thyroid tissue. The best results can certainly be obtained with repeated implantation of small scraps, and for this it is better to implant the scraps in the subcutaneous tissue (Christiani) or in the peritoneal tissue (von Eiselsberg). H. Salzer (Wiener klin. Woch., March 18, 1909; Jour. Amer. Med. Assoc., April 24, 1909).

Series of personal experiments in thyroid implantation showed that thyroid tissue of the guinea-pig transplanted in the same animal heals most easily and best when the transplantation is made into the subcutaneous connective tissue; likewise, the peritoneal cavity shows itself a very favorable implantation site; that transplantations into the spleen heal fairly well, but the end results are less good and not so certain as those obtained when one uses as implantation sites the two places above named; the liver and the bone-marrow are very unfavorable organs for the healing in the thyroid tissue; that thyroid transplantation promises in general more fruitful results if one avoids all bleeding in the pocket destined to receive the graft; that if one transplants the thyroid tissue in conjunction with the connective-tissue capsule pertaining to it it is to be observed that the follicles in the vicinity of this capsule are better preserved and more numerous than the more remote follicles; that the best results are attained if one transplants into the subcutaneous tissue very thin slices of thyroid tissue instead of larger pieces; one condition is that one of the surfaces of the implanted piece is covered by the connective-tissue capsule of the thyroid. Carraro (Deut. Zeit. f. Chir., Feb., 1909).

Obesity.—The treatment of this condition by means of thyroid preparations was far more in vogue a few years ago than at present, owing mainly to its indiscriminate use by laymen, and to the use of excessive doses by the profession. Both these features were the cause of dangerous phenomena (and sometimes death) during the course of treatment, or of pernicious after-effects. When thyroid preparations are used intelligently, however, adjusting the dose to the needs of each case, and regulating judiciously the concomitant diet—which in some cases means an increase—a great deal of good may be done in the great majority of cases, besides improving the appearance of the patient and his general well-being.

The cases in which thyroid preparations act favorably are those in which metabolic activity, especially its catabolic phase, is deficient. The fat, ruddy boy or the plethoric, vigorous, red-

faced high-liver do not belong to this category. Those that do are pale, flabby, anemic, in most instances females between 25 and 45 in which the heart beat is weak, sometimes irregular and rapid with compressible pulse The fat in such is more or less irregularly distributed in the subcutaneous tissues; they suffer from dyspnea, especially on exertion, and fall asleep readily at any time. Such cases are in reality instances of mild myxedema in which the thyroid does not supply quite enough secretion to satisfy the needs of the organism. It is not a question of overeating with them; such patients, in fact, are, as a rule, abstemious, the slowness of their tissue exchanges causing them to have but little appetite. Unable to burn up their carbohydrates, sugars, starches, and fats as fast as they are ingested, fat steadily accumulates in all tissues.

Thyroid preparations, when judiciously used under such circumstances, are of value mainly because the rôle of thyroid secretion they replace is precisely—from my viewpoint—to enhance the catabolic phase of metabolism, essentially the function at fault in obesity. The fat-cell is rendered more susceptible to oxidation—along with the other tissues—and the excess of fat is steadily consumed.

Series of about 100 cases of **obesity** in which thyroid extract was used. No untoward symptoms were noticed in any of the cases, malaise, headache, palpitation, and nervous derangement being entirely absent. Albuminuria was not seen at any time. The thyroid gland used in all instances was B. W. & Co. tabloids. The initial dose was 2½ grains with each meal, either mixed with the food or taken with a little water. After seven days the dose was increased to 5 grains with each meal, and this dose was not increased in any case. The tabloids were crushed before being taken. In the successful cases summarized below no alteration in diet was ordered, the patient eating and drinking anything he or she desired. Alcohol was, however, strictly prohibited in any form.

Of 78 females treated 69 were between 25 and 45; their average weekly loss was 2½ to 4 pounds, and the result was permanent cure; 9 were between 15 and 19, and there was no permanent result in any of them. Of 25 men 9 were between 30 and 47; they lost on an average 2 to 3½ pounds weekly; the cure was permanent; 11 men between 30 and 47 lost 1 to 1½ pounds on an average, but the result was not permanent; on 5, between 14 and 17, there was no effect at all. W. J. Hoyten (Brit. Med. Jour., July 28, 1906).

In the treatment of constitutional **obesity** the writer uses Merck's thyroid-gland tablets containing 0.1 gram of gland. One to 2 tablets are given daily during the first three to four days, and during the following eight to ten days the dose is increased to 3 tablets; in very exceptional cases as many as 4 tablets may be given. The dose is now decreased to 2 tablets for the following eight days, and then to 1 tablet for another five to eight days, after which a pause of eight days is allowed before recommencing the treatment on the same lines. This pause must be made, as in every case after-effects occur, lasting some time. After two or three courses of treatment a longer pause, extending to about three months, may be made; its duration depends upon the patient's weight, which should be frequently ascertained. C. Pariser (Zeit. f. Aerztl. Fortbildung, Nu. 5, 1911).

Contraindications to the use of thyroid preparations in obesity have been elaborated by various observers; but perusal of their work indicates clearly that they have been administering excessive doses. Such doses are always dangerous in the obese, since the heart

is itself invariably fatty, while, conversely, small doses are always helpful because they very gradually rid the heart of the fat which compromises its functions and eventually causes death when the patient has not been carried off by some intercurrent disorder. Even moderate doses have not proven harmful when the patient was under medical surveillance.

The *dose* of desiccated thyroid need not exceed 1 grain (0.65 Gm.) three times daily in any case. This suffices to cause a decrease of weight of from one to three pounds a week, and sometimes more, Anders ("Practice," 8th ed., p. 1276) having observed in 2 cases under this dose "a progressive loss of weight at the rate of 4 to 6 pounds per week, respectively, without injury to the general health." Such doses do not impose upon the patient the need of modifying his usual mode of living, and his diet need not, unless excessive, be altered. When the obesity is accompanied by weakness, the appetite is usually increased, especially when, as is my custom, gr. $\frac{1}{50}$ (0.0012 Gm.) of strychnine is given with each dose of desiccated thyroid. The patient does best under these conditions when lean meats, plainly broiled, roasted, or stewed, constitute the increase of his dietary. This treatment is valuable in another direction: it tends to counteract any tendency to constipation that may be present.

Danger signals or *untoward effects* are not met with when small doses are given, as previously stated, but the physician has occasionally to treat some victim of excessive dosage.

> Case in which a man took for obesity nearly 1000 5-grain tablets of thyroid extract within five weeks. After the first three weeks he began rapidly to develop the symptoms of acute Graves's disease. When thyroid was stopped and patient was put upon arsenic all the symptoms disappeared quickly, excepting the eye changes and the goiter, which were still notable for about six months. A. V. Notthaft (Centralbl. f. innere Med., April 16, 1898).

The untoward effects most frequently met with in obese subjects are of cardiac origin: marked discomfort in the precordia, dyspnea with tendency to heart-failure. In some instances this has been followed by death when marked fatty degeneration happened to be present. But, as stated, these do not occur when small doses—1 grain (0.065 Gm.) of the desiccated thyroid—are used. Even the greatest watchfulness will not prevent toxic effects when large doses are administered, since the accumulation of the thyroid principle proceeds at a rapid rate and the milder symptoms of thyroidism are almost at once followed by its acute manifestations—those previously described.

Miscellaneous Disorders.—In the foregoing diseases thyroid treatment may be regarded as a specific, none other affording satisfactory results. Its use is being extolled in many other disorders; but it is still a question whether it procures better effects or even as good results as other available remedies. These will be considered in their alphabetical order.

Acromegaly.—The reports of cases of this disease treated with thyroid have been insufficient to warrant a conclusion, the results having been contradictory. This is probably due to their empirical use. According to my interpretation of the disease: hypertrophy of the pituitary causes excessive activity of the adrenals and thyroid (which

the pituitary governs) for a time, *i.e.*, during the *sthenic* period of the disease. Given during this period, thyroid preparations can only, therefore, add fuel to the fire and do harm. There comes a time, however, usually after several years, when the enlargement of the pituitary ceases and degeneration of this organ occurs, initiating the *asthenic* period. The adrenals and thyroid then usually reduce their functional activity inordinately, and oxidation and

Case illustrating the association of acromegaly and goiter. (*G. R. Murray.*)

metabolism are inadequate for the perpetuation of the vital functions. Here thyroid (preferably with adrenal) is useful and may serve greatly to prolong life.

Case of **acromegaly** treated with dried thyroid extract in gradually increasing doses until 12 grains a day were taken, besides galvanism and tonics. Three months later she was feeling very much better, her memory had improved, and she spoke and moved more rapidly. She had lost over 20 pounds in weight, but felt stronger. General condition practically the same. The history of the case and the marked physical changes leave little doubt that it was a case of acromegaly, but certain anomalous symptoms—such as the puffy conditions of the eyelids, which may, however, have been simply the result of anemia, though its appearance was somewhat different; the slow speech, and the altered mental state—suggested that her condition was also associated with a loss of function of the thyroid gland. G. G. Sears (Boston Med. and Surg. Jour., July 2, 1896).

Case of a woman 26 years old who had suffered from **acromegaly** for upward of two years, and who for a period of five months had been treated with mixed pituitary and thyroid extracts, with great improvement. The superficial resemblance between acromegaly and myxedema seemed to justify the administration of thyroid extract, especially as in several cases of acromegaly treatment with pituitary extract alone had failed to effect any improvement. Rolleston (Brit. Med. Jour., April 17, 1897).

Arteriosclerosis.—As is well known, the iodides are used with benefit in this condition. It naturally follows that thyroid preparations, which owe their therapeutic activity to the iodine in organic combination they contain, should likewise prove beneficial. This proved true in cases reported by Lancereaux (La Semaine méd., Jan. 4, 1899), James Barr (Brit. Med. Jour., Jan. 20, 1906), and other authorities. The favorable action of thyroid in these cases, however, necessitates the use of large doses—5 grains (0.3 Gm.) three times a day—enough to cause general vasodilation. As such doses are unsafe in aged subjects, who constitute the greatest proportion of our cases, its use should be limited to middle-aged patients, therefore, reserving the iodides for the former. Sir James Barr, in fact, considers iodine more valuable than thyroid preparations.

Arthritis, Chronic Rheumatoid.—In this disease good results are occa-

sionally obtained when no other agent will produce the least effect. Léopold-Lévi and de Rothschild, for example, describe the phenomena observed in 2 cases of chronic rheumatism with hydrarthrosis in which thyroid extract proved of distinct value. In 1 of these the hydrarthrosis followed a fall from a bicycle, and was the precursor of attacks of muscular rheumatism, all the joints being gradually involved in the morbid process. Notwithstanding seasons at Aix-les-Bains, Dax, and other stations, the patient became quite impotent, having even to be fed. The usual remedies proved unavailing, though aspirin and iodine seemed, at least for a while, to be of some benefit. The patient's condition becoming steadily worse, thyroid extract was tried, beginning with 1½ grains every other day during ten days, followed, after five days, by resumption of the remedy; then giving again only 1½ grains every other day. This dose was gradually increased until, eleven months later, the patient was taking 7½ grains, in divided doses, daily. Good results have also been recorded by Revilliod, Lancereaux, and others.

The beneficial effects of the drug become self-evident when its action and the pathogenesis of chronic rheumatism are interpreted from my standpoint. Briefly, while I have ascribed this disease to "inadequate catabolism of tissue wastes, and excitation, by the toxic products formed, of the vasomotor center" thyroid extract, as stated in the foregoing pages, enhances general oxidation and the destruction of wastes, by increasing the blood's asset in opsonin and autoantitoxin.

Thus, increase of appetite was the first effect noted in the cases referred to above; this is a normal result, since the greater cellular activity and catabolism created a greater demand for foodstuffs. Increased heat production soon replaced the marked and constant chilliness from which the patient suffered—an effect due to the marked increase of oxidation the thyroid extract engendered throughout the body. The dose was increased to 1½ grains one day, then to 3 grains the next, this being continued ten days. After a period of rest of five days, 3 grains were again given daily. The pain became less—a fact due to decrease of the vascular tension, owing to increased destruction of the toxic wastes which, as I have pointed out elsewhere, excite the vasomotor center, thus causing constriction of all arteries. The sensory nerve-terminals being relieved of the hyperemia which caused the pain, the latter became less marked in proportion. Closely connected with this beneficial action was the effect on the joints, viz.: the *hydrarthrosis became reduced*. Being also due to excessive vascular tension, it is plain that by causing vasodilation, in the manner just explained, thyroid extract caused the excess of fluid to leave the joints. The dose being still further increased until 7½ grains were taken daily, *emaciation* occurred—a well-known effect due to excessive catabolism provoked by large doses of thyroid extract.

Eleven months' treatment brought Léopold-Lévi and de Rothschild's case back to a condition of comfort, the joints having resumed their shape and flexibility—with the exception of one knee, which remained ankylosed—owing doubtless to fibrosis, a condition beyond the reach of the remedy. This does not militate against its use, however; it simply shows that the treatment was resorted to too late to avoid

irremediable organic lesions. The authors, in fact, refer to a case treated by Parhon and Papinian (Presse méd., No. 1, p. 3, 1905) in which thyroid extract had produced, though the disease was of twenty-four years' standing, "a true regeneration." When 7½ grains (in five divided doses) daily had been given some time, palpitations, tachycardia, and arrhythmia appeared. On withdrawing the remedy these untoward effects ceased, but recurred as soon as its use was resumed. This affords additional evidence in support of a fact I have often emphasized, viz.: that the beneficial effects of thyroid extract are obtained only when small doses are used.

Case of **rheumatoid arthritis** in which most of the ordinary methods of treatment for the condition were tried without any beneficial result. Finding on examination that her thyroid was small, the writer commenced giving thyroid extract, 2 grains three times a day, and after a week four times a day. In about two months all the pain and nearly all the swelling had gone from both knees; there was no fluid in the left knee and hardly any in the right knee. A week later there was no fluid in the right knee, and in a few days more all the swelling had disappeared. G. Steele-Perkins (Lancet, March 5, 1910).

Case of **rheumatoid arthritis** in which the writer was struck by the patient's rough, dry, harsh skin, crisp hair, husky voice, and deep suprasternal notch; the prominence of the trachea, and apparent absence of thyroid gland, analogy to other conditions suggesting deficiency of thyroid secretion.

Accordingly, the extract of thyroid was administered in doses of 5 grains three times daily, together with adjuvant treatment to be mentioned presently. In a month the results were remarkable. The patient could struggle on crutches from one room to another, his appetite returned, and pain was almost gone. In three months he could walk with two sticks, and in eighteen months he was able to walk three miles with the aid of one stick. His elbows and shoulders have regained their mobility almost entirely, and he has been for a year able to do without his thyroid extract without a relapse. At the present date he is able to get about well, with slight flexion of one knee and some metacarpophalangeal deformity, but is fat and well.

Two additional cases in which marked improvement occurred. In the writer's opinion the group of cases likely to receive benefit are those in which changes are chiefly confined to the synovial membranes, without erosion of cartilage or eburnation of bone, such cases in fact as Schüller describes as "chronic villous arthritis." Wilson (Brit. Med. Jour., Dec. 10, 1910).

Cancer.—Thyroid preparations have been tried by a number of clinicians in this disease. Some have obtained favorable results; others observed only temporary benefit; others again have observed no effect whatever.

In the first place, thyroid preparations should be used *only in absolutely inoperable cases,* surgery having given far better results than any other method, including X-rays and thyroid preparations. In the second place, it is a mistake to attribute specific or even curative properties to thyroid preparations alone. They only assist in the curative process by facilitating proteolysis, *i.e.,* breaking down of the growth. The detritus is such that after its use the kidneys are greatly exposed, and cases have been reported in which fatal nephritis followed the use of large doses. Such doses are, therefore, dangerous. Small doses do quite as well; but even when these are used the patient should be ordered to drink at least one quart of water daily, preferably a mineral water, to promote

flushing of the kidney and thus facilitate the elimination of toxic wastes and detritus. One or 2 grains of desiccated thyroid three times daily usually suffice, but 3 grains can be given if no rise of temperature is observed.

Case of multiple **carcinoma of the skin** and subcutaneous tissue in a widow aged 61. The original growth had been removed a year before the author saw the patient, but other growths had since appeared, and the patient's health was declining. Thyroid medication was tried, starting with 5 grains daily, gradually increasing to 10 grains, and finally to 15 grains, daily. The patient quickly showed signs of improvement; the palpitation, sickness, and emaciation gradually disappeared *pari passu* with the gradual disappearance of the growths. In less than three months the growths had entirely disappeared, the patient was practically well, and had recovered her lost weight of 3 stone. This occurred in 1901, and at present the patient is still well and has not suffered since. The writer summarizes other and similar cases from medical literature. E. Hughes Jones (Brit. Med. Jour., Feb. 25, 1911).

Case of **cancer of the larynx**. The patient was a man 51 years of age who developed malignant disease of the larynx for which total extirpation of the larynx was done. After an attack of secondary hemorrhage the patient finally began to recover on the sixteenth day after the operation and gradual healing occurred. About three months later, a mass of glands over the right carotid sheath were found to be secondarily affected, and these were removed. He kept well for eight or nine months after this operation, and then recurrence of the growth took place and a lump as large as a walnut developed on the right side of the neck. An attempt was made to remove it, but it was found at the operation that the growth involved not only the common carotid artery, but the prevertebral muscles. Complete removal could be accomplished only by exposing a healthy portion of the common carotid, ligating it, and dissecting the cancerous mass up from below and sacrificing the pneumogastric nerve, an operation that would almost certainly have been fatal, while it gave little or no prospect of eradicating the disease. The lower portion of the mass involved the thyroid gland. Accordingly, the operation was abandoned except that a small portion was removed for microscopic examination. This proved to be cancerous. A few days later, the patient was seen on consultation with Sir Charles Ball, who suggested that thyroid extract should be given and cited 2 cases of inoperable cancerous lymphatic glands in which that remedy had been tried with success. Three-grain doses of the extract were prescribed three times daily. At the end of four months' treatment, there was distinct diminution in size of the glands. The thyroid extract was continued with the result that the growth finally disappeared completely, and the patient became quite well.

There is now a series of well-authenticated cases of cancerous recurrences on lymphatic glands cured by thyroid extract. R. H. Woods (London Letter, N. Y. Med. Jour., July 22, 1911).

The other agents indicated as such as would be warranted were the same general symptoms met in other disorders. The anemia, which, with the general vasodilation and the resulting recession of blood from the surface, gives the patient the waxy pallor sometimes observed, should be met by iron, preferably Blaud's pill, and strychnine in full doses. In personal cases, by treatment based on general principles, using thyroid only when the growths seemed to take a fresh start, they have been kept in abeyance several years, six years in one case, four years in another.

The same treatment is indicated in cases after operation to prevent recur-

rence, the aim here being to enhance the functional activity of all organs, including those which govern the immunizing processes. General tonics, especially iron and strychnine, and out-of-door life are of especial value in this connection.

Cutaneous Disorders.—After a prolonged trial of thyroid preparation in many diseases of the skin, dermatologists have come to the conclusion that they were indicated in disorders due to deficient metabolism. As recently stated by Winfield, these include the erythematobulbous type, which includes **dermatitis herpetiformis**, and the psoroeczematous type, to which belong **prurigo, psoriasis,** and **chronic eczema.**

This is fully accounted for by the action of thyroid products on oxidation and metabolism I have described. This is well shown in the effects noted by Don: 1. Increased nutrition of the skin; hence its probable remedial action in ichthyotic conditions: an effect produced without any necessary abnormal perspiration. 2. Increased action of the cutaneous glands, accelerating excretion of waste products, thus keeping the surface in a supple condition. 3. Regrowth of hair, as shown in myxedema and some cases of general alopecia. 4. Increased activity of the epidermal layers, causing desquamation of unhealthy epidermis and reproduction of a new covering, as observed in ichthyosis, psoriasis, dry chronic eczema, and also in some cases of myxedema and cretinism.

Series of consecutive cases of **eczema** in young children successfully treated by thyroid. In the first case, 14 months old, the baby had suffered from eczema of the face for nearly a year. This had been entirely resistant to the usual applications and internal treatment, nor was hospital treatment more efficacious. Two and a half grains of a thyroid tablet were given daily. In a little more than one month the child was entirely well. His cure persisted for nearly a month, when the disease showed a tendency to recur. The second course of thyroid was followed by a permanent cure. The 4 other cases gave similar results. Eason (Scottish Med. and Surg. Jour., May, 1908).

Two cases of **eczematous seborrhea** successfully treated with thyroid. In the first case the scalp was normal at the end of two weeks; in the second in one month. Complete cure occurred in both cases, and has persisted. Moussous (Archives de méd. des enfants, March, 1908).

It is pretty certainly established that preparations from certain ductless glands exert a marked influence upon those **dermatoses due to faulty metabolism.** There is a certain class of skin diseases, those belonging to the erythematobullous type and those of the psoroeczematous variety, in which the preparations coming under the head of animal therapy seem to do the most good. J. M. Winfield (Interstate Med. Jour., Nov., 1909).

In **psoriasis** thyroid is harmful when the eruption is developing, but it sometimes acts with surprising efficacy in fully developed cases. The untoward effects observed by dermatologists, however, are in great part due to the fact that they use too large doses. These, as previously stated, enhance catabolism violently and increase the waste products in the blood and, therefore, the cutaneous disorder.

Five cases of **scleroderma** in 4 of which the thyroid was small and atrophied, while in the other the thyroid was large and hard. Thyroid treatment gave good results in the 2 in which it was applied, commencing with small and progressive doses. None of the patients presented signs of nervous changes suggesting atrophic origin, but

everything confirmed the assumption of some connection between the cutaneous affection and the thyroid gland. Pedrazzini (Gaz. degli Ospedali, Aug. 1, 1909).

Thyroid has been tried in **lupus** by a number of observers. Though the results were contradictory, the bulk of the evidence indicates that it is worthy of further trial. Owing to its influence on oxidation, thyroid enhances the nutrition of the skin and thus antagonizes the destructive process while promoting that of repair. As full doses have to be used during a prolonged period, the patient should be carefully watched. Thyroid has been tried in **leprosy**, but the results were not encouraging, though the remedy was pushed as far as safety would allow.

In a case of **hypertrophic rosacea** which has resisted all forms of treatment, Isadore Dyer, of New Orleans, used thyroid with, for local use, a salve containing resorcin, ℈j; rose water, ℥iv; lanolin, q. s. ad ℥vj. After two months there was decided improvement, the skin being soft and normal to the touch and the color greatly improved. The patient was discharged cured after three months of thyroid medication.

Case in which thyroid treatment was commenced at the age of 5 months; in two months the congenital **ichthyosis** subsided, and in two months later it had entirely disappeared. After suspending the thyroid treatment, a preparation of arsenic was given. The ichthyosis returned, but yielded again to the resumption of the thyroid treatment. In another child, in which there were also signs of myxedema, very favorable results were obtained from the thyroid treatment. Certain cases of ichthyosis ascribed to inherited syphilis are really of thyroid origin, the thyroid lesion being possibly secondary to syphilis. Weill and Mouriquand (Presse méd., Feb. 17, 1909).

Case of **elephantiasis** of ten years' duration in which genuine reduction in size of epithelial overgrowth followed each attempt at thyroid administration, but intervals of arsenical treatment seemed necessary to correct the severe constitutional results of the animal extract. Within seven months the patient lost 11 kg. of body weight and the feet were markedly reduced, the right nearly twice as much as the left one. The patient suffered two illnesses of the respiratory tract during thyroid administration, an attack of pleurisy and an attack of pleuropneumonia about five months later. The observer suggests thyroid treatment for other dermal morbid processes of a hypertrophic character. F. M. Baca (El Observador Médico, vol. v, No. 4, p. 48, 1909).

Exophthalmic Goiter.—The results of treatment by thyroid preparations have been variable. In one case, thyroid will produce marked benefit; in an apparently similar case, it will do considerable harm. In truth, there are distinct stages of the disease, which become evident in the light of the rôle I have ascribed to the thyroid, viz.: that of increasing the vulnerability of all phosphorus-laden cells, including waste products, to oxidation, and facilitating (as opsonin) their destruction by the defensive constituents of the blood, including its phagocytes.

With this function before us, what can we expect from thyroid preparations in a case of exophthalmic goiter in which the excretion of phosphoric acid is excessive (sometimes ten times the normal, according to Scholtz) and other evidences of excessive oxidation are present? Obviously none. Here a toxemia prevails, probably of intestinal origin, in which the toxics excite the adrenothyroid center. The thyroid and its mates, the adrenals, being stim-

ulated abnormally to increase the antitoxic power of the blood, the thyroid becomes enlarged, and the excess of secretion (added to a corresponding excess of adrenal secretion) produces the general symptoms of the disease. It is obvious that in these cases thyroid preparations can only do harm, and that the arrest and prevention of intestinal autointoxication, by suitable aperients and a proper semimilk diet and physical rest to reduce muscular wastes to a minimum, are indicated.

There comes a time, however, when in this identical case the thyroid and adrenals, overworked during a period of years, steadily lose ground and become the seat of organic changes which inhibit below normal their secretory activity. The thyroid remains large, and the tachycardia continues: The latter is no longer due to excessive oxidation and stimulation, but to the opposite condition, a prominent feature of which is low vascular tension. In these cases there is produced what virtually amounts to a myxedema—all the symptoms of which are sometimes observed. Thyroid preparations are then productive of much good.

> Case in a child of 4 years who six months previously had developed goiter, exophthalmos, and tachycardia. For eighteen months had had convulsions, and since the onset the symptoms had been much aggravated by an attack of whooping-cough. Strophanthus, bromides, and salicylate were given with no result, and the child's condition was deplorable, when it was put on thyroid extract, 1 pill of 0.1 Gm. (gr. ij) a day. From this time there was steady improvement in the condition. The authors also witnessed cases in which thyroid had done great harm. Leroy and Variot (Le progrès médical, Dec. 14, 1901).

In some cases, however, the causative toxemia is of a kind which can be counteracted by means of thyroid preparations; those in which, owing to the more or less sudden accumulation of catabolic products or the retention of such in the blood, the thyroid becomes enlarged owing to excitation of its center. This is a pseudotype of exophthalmic goiter, resembling pathogenically the thyroidal enlargement observed in the pregnant woman, and due to the excess of waste products in her blood incident to the presence of the fetus. There may be slight tachycardia in these cases, but the other symptoms of exophthalmic goiter are absent. It coincides sometimes with delayed menstruation. In some cases the thyroidal enlargement comes on suddenly, and may be sufficiently severe to obstruct breathing by compressing the trachea. In all such cases thyroid preparations afford decided benefit and may prove curative.

Of value in this connection and in the same class of cases as thyroid preparations is the Rogers-Beebe cytotoxic serum, prepared by injecting purified nucleoproteids derived from the thyroid into animals of alien species. This, according to Rogers, gave 23 cures in 90 cases, while 53 were improved. Here, from my standpoint, the serum acts as antitoxin in the destruction of the poisons which, by exciting the adrenothyroid center, cause the disease.

> Results obtained in 16 cases treated by the serum: 5, or 31 per cent., have been cured, the oldest case having been without symptoms for over three years, the last for about six months. One of these cases was very toxic, her pulse being over 180 on exertion, and with a great deal of nausea and diarrhea. Within six weeks she was practically relieved of all subjective symptoms, her

pulse being reduced to about 80. Seven, or 44 per cent., were markedly improved so that their life had been rendered much more comfortable, and this improvement apparently is permanent. Two of these cases were very serious ones, and 3 have taken the serum treatment twice, with an additional improvement the second time. Four, or 25 per cent., do not appear to have made any permanent improvements, though all of these were certainly better while under the direct charge of the authors, but relapsed more or less promptly after being sent home. Only 1 case treated has died. McCaw Tompkins (Old Dominion Jour. of Med. and Surg., Oct., 1909).

Thyroidectin, a preparation representing the blood of the thyroidectomized animals, is supposed to antagonize the excessive production of thyroid secretion, but the reports have been conflicting. It is probable that it should be used only during the first or sthenic stage of the disease—if the theory of its sponsors is sound.

The writer has treated 7 patients with thyroidectin; 3 of the cases were very severe. In each of these cases rest in bed, the ice-bag to the heart, and other remedies, such as sodium phosphate or strychnine, have been used more or less regularly. All the patients improved, but he could not see that the process was more rapid or otherwise different from those treated without thyroidectin, but the same in other respects. Dock (Amer. Med., Feb. 24, 1906).

Goiter.—In the majority of cases of goiter we are dealing, from my viewpoint, with a result of overactivity of the thyroid mechanism. This may be due either (1) to the presence of some toxic (derived mainly from contaminated water) in the blood, which excites the adrenothyroid center or (2) to absence in the air or in the water or foods ingested of the iodine necessary to supply the thyroid the proportion it needs to elaborate its secretion.

In children and young adults iodine or thyroid preparations are frequently beneficial, therefore, whereas in adults in which organic changes have occurred in the enlarged gland they are seldom of use, as far as material reduction of the goiter is concerned. In any case, very small, even fractional doses should be given at first, whether thyroid preparations or iodine be used, gradually increasing the dose if need be. I have seen a minute dose of iodine produce untoward effects. Cases in which evidences of myxedema and hypothermia are present usually stand normal doses without discomfort.

Effect of iodine on natural, colloid, and actively hyperplastic (parenchymatous) thyroids of dogs. Numerous forms of iodine and iodine-containing substances were used in different ways. Very small amounts were necessary to induce thyroid changes. The more marked the hyperplasia, the greater is the amount of iodine taken up. Iodine, administered to dogs with hyperplastic thyroids, acted like the desiccated thyroid itself, and very beneficial results were obtained by the use of very small doses gradually increased in these hyperplastic conditions. Marine and Lenhart (Archives of Intern. Med., Sept., 1909).

Series of 6 cases in which unusually small doses of sodium iodide in patients with goiter induced symptoms of intoxication, the patients all presenting the familiar picture of hyperfunctioning on the part of the thyroid instead of the anticipated benefit. The total amount given in the course of the treatment ranged from 1 to about 7 Gm. (15 to 100 grains) in the course of from ten to forty-five days, the daily dose being from 0.09 to 0.33 Gm. In 1 patient the thyroidism developed after 10 daily doses of 0.1 Gm. (1½ grains). Analysis of the cases showed that the patients were all from families with a

tendency to exophthalmic goiter, or diabetes, or neuropathies. Pineles (Wiener klin. Woch., March 10, 1910).

Hemophilia.—Thyroid preparations are extremely valuable in this dyscrasia, due to a deficiency of fibrin ferment in the blood. As this body, according to my researches, is mainly composed of the adrenal product, the increased functional activity of the adrenals provoked by thyroid preparations administered increases the blood's asset. The coagulation time in hemophilia may be brought down from over ten minutes to three or four minutes in adults by 3-grain doses of the desiccated thyroid three times daily after meals. This is effective not only in the treatment of the disease, but also when operations are necessary in hemophilics. Even such operations as removal of a kidney have been resorted to with perfect safety after the coagulation time had been reduced to three minutes.

Case in which **hemophilic epistaxis** was absolutely unaffected by ordinary therapeutic agents, and the epistaxis became so persistent and exhausting that permanent blocking of the nasal fossa was necessary. Treatment by thyroid extract exerted an immediate and beneficial effect, and was followed by cure. In three days the violent and persistent epistaxis had practically stopped. In six days, about 8 grains of thyroid extract having been given daily, the purpuric eruption ceased. Scheffler (Archives de méd. et de pharm. Mil., March, 1901).

Three cases of **operations in "bleeders"** in which the administration of thyroid extract, for some days preceding operation, as advised by Sajous, was followed by remarkable results in lessening the hemorrhage at that time. Sajous holds that the thyroid extract stimulates the anterior pituitary body, which in turn excites the adrenals to greater activity, thus augmenting the proportion of fibrin ferment in the blood, and consequently its coagulating power. This explains the action in these hemophilics, and its use is recommended as a preparatory treatment whenever surgical operation is to be undertaken in such persons. W. J. Taylor (Monthly Cyclo. of Pract. Med., July, 1905).

Incontinence of Urine.—In a large number of these cases, the enuresis is due to general asthenia, and the muscular debility which attends this state carries along with it inability of the sphincters to perform their functions at all times, especially when during sleep general relaxation prevails. The influence of thyroid on general metabolism and nutrition and the resulting increase of functional power in all organs affect equally both the cystic and urethral sphincters and thus overcome the trouble. The doses should be small in order to enhance general nutrition.

Nocturnal incontinence of urine in young children and adolescents is due to thyroid insufficiency. Several cases in which the use of thyroid extract was followed by improvement or cure. Children who suffer from incontinence are almost always undersized, and they present the infantile habitus in varying degrees—improperly placed teeth, naso-pharyngeal adenoids, flat chests, and emaciated and slender extremities. Such patients are often flat-footed and their feet have an offensive odor, their gait is stiff, they suffer from pains in the thighs and from sciatica produced by the cold and moist surroundings in which they lie at night. The systematic examination of the urine in these cases shows an abundant deposition of the cells covering the free surface of the mucous membrane of the bladder. In children beyond 2 years of age the writer gives 3 5-grain tablets of thyroid *per week*, with from 3 to 5 grains of potassium iodide and bromide daily. Hertoghe (Bull. de l'Acad. Royale de méd. Belgique, xxi, No. 4, 1907).

Case in which the writer had the adenoids of a 9-year-old boy removed, hoping it would cure him of **nocturnal incontinence.** It made the boy much worse, however, and, believing that the removal of the adenoids deprived the boy of a necessary internal secretion, he then gave him thyroid extract, ½ grain twice daily. The result was instantaneous and complete, the boy no further wetting the bed. Twenty-four other cases were thus treated, with but one failure. Williams (Lancet, May 1, 1909).

Infectious Diseases.—So far thyroid preparations have not been used to any marked extent in this class of disorders, but it is probable that they will eventually prove of great value owing to the identity of the thyroid secretion as *opsonin,* pointed out by myself in 1907, as previously stated. Several investigators, including Marbé, of the Pasteur Institute, have since found that the administration of thyroid preparations to animals increased the opsonic power of the blood.

There are autoinfections which develop within the organism as the result of weakening of the organic defensive forces and exalted virulence of the ordinary saprophytic microbes. It is probable that certain specific infectious diseases, such as diphtheria, typhoid fever, and others, are likewise of autogenic origin. The organism is constantly fighting against its parasites, by weakening them and finally destroying them through the phagocytes. The opsonins of the tissue juices and exudates, by acting upon the microbes and upon phagocytosis, assist in the natural defenses of the organism. These opsonins, which seem to become one with the alexins, are to a considerable extent the product of the thyroid gland. Stepanoff (Thèse de Paris, 1908).

"Sajous has attributed, among the functions of the thyroid body, a rôle to the latter which he assimilates to that of opsonins and to autoantitoxins. More recently, Miss Fassin, M. Stepanoff, and M. Marbé have confirmed on their side the influence of the thyroid on the blood's asset in alexins and opsonins." ("Physiopathologie du Corps Thyroide," p. 20, Paris, 1911.)

The enlargement of the thyroid, which can be distinctly detected by palpation, and its erethism during infectious and other toxemias indicate that it fulfills active functions in the immunizing process.

After removal of the thyroid gland the urine contains a greater percentage of poisonous matter than that of healthy animals does; the urotoxic coefficient begins to rise gradually, even before the nervous symptoms attributable to the operation set in; animals that are kept without food also show an increased toxicity of the urine; the administration of thyroid juice is capable of first moderating the increment of urinary toxicity and then reducing the toxicity; accordingly, in the organism of a dog that has been deprived of the thyroid gland there are toxic materials in excess, and thyroid-gland juice serves to neutralize them. De Lucca and d'Angerio (Rivista medica therapeutica, No. 9, 1896).

There is hypersecretion of colloid substances in the gland in acute or chronic infective diseases, as well as marked epithelial proliferation and an abundant neoformation of glandular tissue. Interstitial inflammatory processes, such as abscesses and tubercles, are rarely met within the gland. The colloid substance has the property of destroying micro-organisms. The epithelial proliferation and the hypersecretion of colloid substances are due to a toxic product of the infective process, perhaps caused by destruction of the micro-organisms by colloid substance, or brought to the gland by the circulating blood. Odoacre Torri (Il Policlinico, May 15, 1900).

Examination of 55 thyroids of which 38 were taken from persons dead of infectious diseases. As a means of comparison 17 were taken from persons in

whom death was due to other causes. Of the infectious diseases thus studied 6 were diphtheria, 6 scarlet fever, 5 miliary tuberculosis, 5 measles, 4 fibrinous pneumonia, 3 puerperal fever, 2 typhoid fever, 2 septicemia, and 5 pulmonary tuberculosis. In the majority of infective diseases the interstitial lymph-vessels show an accumulation of colloid material. S. Kashiwamura (Virchow's Archiv, Bd. 166, H. 3, 1901).

Thyroid feeding renders white mice much less susceptible to the toxic action of acetonitrile, but has no effect on the toxic dose of sodium nitroprusside or of hydrocyanic acid. This indicates that the thyroid preparation does not act by increasing sulphur compounds by metabolism of proteids, but by some specific antitoxic power. Proteids (such as casein, nutrose, peptone), nuclein, and preparations of the thymus and of the suprarenal glands counteract to some extent the neutralizing or protective power of thyroid gland against acetonitrile. Thyroidectin increased slightly the susceptibility of mice to acetonitrile. Reid Hunt (Jour. of Biol. Chemistry, vol. i, No. 1, 1906).

In infectious diseases a slight swelling of one or both lobes is common, pain being elicited by the pressure of the fingers. In acute articular rheumatism it was found in 53.6 per cent. of cases. It is also found in typhoid fever, measles, scarlatina, secondary syphilis, mumps, and other diseases. Curiously, however, it is absent in many grave infectious diseases, such as septicemia, ataxoadynamia, and gangrene. It looks as if enlargement of the thyroid in various infections were the expression of a defensive reaction against their pathogenic agents and their toxins. Vincent (Comptes-rendus de la Société Médicale des Hôpitaux, 1906).

[The participation of the thyroid in general immunity pointed out by myself in 1903 and since confirmed, we have seen, explains the overactivity of the thyroid in certain disorders. But, as I have repeatedly employed in "Internal Secretions," vol. ii, this applies only to those diseases which are capable through their toxins of exciting the thyroadrenal center, thus evoking a protective reaction on the part of the thyroid and adrenals. Various toxins and poisons are not only unable to excite this center, but can depress it. Hence the fact that in the conditions mentioned (excepting septicemia, in which Vincent is wrong in his generalization) the thyroid gives no evidence, through tumefaction and tenderness, of overactivity. C. E. DE M. S.]

So far, thyroid preparations have been used in but few diseases. In true **infectious tonsillitis**, desiccated thyroid clears the field promptly. It does so, of course, by enhancing the bactericidal and antitoxic powers of the blood and glandular secretions. The bacteria being rendered more sensitive, that is to say, more easily digestible, they readily become the prey of the phagocytes, which are extremely numerous in the tonsils.

Thyroid gland has also been employed advantageously in **septicemia** and in recurrent **erysipelas**, *i.e.*, in streptococcic infection.

Acute infectious disease, especially scarlet fever, can awaken changes in the thyroid gland, a hyperemia, liquefaction and disappearance of the colloid substance, and desquamation of the epithelium. The connective tissue is not altered. J. Sarbach (Mitt. a. d. Grenzgebieten der Med. u. Chir., Bd. xv, Nu. 3 u. 4, 1906).

Examination of the thyroid gland in 7 cases of septicemia. A hypersecretion of the colloid substance was found to take place coincidently with acute or chronic infections. In the acute cases a marked proliferation of the epithelium was observed, whereas the chronic cases were characterized by an active new formation of follicles with sclerosis of the connective tissue. No bacteria could be demonstrated in the colloid substance. It is probable that the col-

loid substance has a favorable influence upon infectious processes. Monaco (Giorn. Med. del Regio Esercito, No. 1, 1907).

Case of a young woman in whom severe **erysipelas** had recurred twenty-two times and in whom areas of ulceration on both legs had suggested syphilis. Under thyroid treatment the attacks of erysipelas ceased. This suggests that thyroid facilitates immunity against streptococcus infection, as it does in autoinfections, such as recurrent tonsillitis. Léopold-Lévi (Bull. méd., July 29, 1911).

Pulmonary tuberculosis, before the disease is sufficiently advanced to compromise the mechanism of respiration, that is to say, during the *first or incipient stage,* is especially vulnerable to the action of small doses of thyroid. As I urged in 1907, the tubercle bacillus, which is also pathogenic when dead, owes its morbid action to an endotoxin rich in phosphorus; being thus prone to oxidation, while the blood's oxidizing power is enhanced simultaneously, this bacillus is promptly destroyed.

The daily administration of thyroid gland at a time corresponding to or preceding infection with **tuberculosis,** and in such doses as are well borne, causes an energetic acceleration of the metabolism of the organism and modifies favorably the action of the experimental tuberculous and pseudo-tuberculous infection in rabbits. The animals treated with thyroid gland live longer than the control animals, and in some cases life is prolonged indefinitely. Frugoni and Grixoni (Berl. klin. Woch., June 21, 1909).

As stated above, it is only in the incipient stage that, as shown by personal experience, thyroid gland is useful to check the morbid process. Later, it produces exhaustion owing to the excessive catabolism it awakens, even in very small doses.

Insanity.—The idiocy of cretinism and the wonderful improvement that thyroid preparations bring about in young cretins suggest that a direct relationship must exist between the function of the thyroid and the organ of mind, the brain. The functions I have ascribed to the thyroid to increase the vulnerability of phosphorus-laden cells, etc., to oxidation explain this beneficial action. Briefly, the thyroid preparation raises the ability of the cerebral cells to replace the sluggish metabolism and inadequate nutrition of which it has ben the seat to the level of normal metabolism and nutrition. In other words, the cerebral cells, along with those of the entire organism, are caused to burn faster; the vital process being correspondingly more active, the function of the brain, as the seat of mental processes, is sooner or later in young subjects carried on with adequate vigor.

Andriezen, of London, who has investigated autotoxis in relation to **insanity** and especially acromegaly, called attention to an important diathetic class of insanities which the textbooks as yet have not recognized. "He did not refer to the so-called gouty or rheumatismal insanities, but to those associated with, and growing in the soil of, myxedema and acromegaly, with a very constant and distinct physiognomy of their own, and a pathogenesis that could be harmonized and well explained by the morbid changes present, changes which lay at the root of the mental as well as the bodily conditions. In the one case (myxedema), a morbid process starting from the thyroid gland affected the whole capacity of the blood in regard to its power of taking up oxygen from the air. On examining the blood with the mercurial pump it was found that its oxygen and carbonic acid were much diminished, and by placing the individual in the apparatus for examining the gases of respiration it was

found out that he took in but little oxygen and correspondingly gave out but little carbonic acid during life. Thus he suffered from weakness and dullness, from subnormal temperature, and from a tendency to the accumulation of incompletely oxidized bodies (fat, etc.) in his tissues." A. McLane Hamilton (Medical Record, April 29, 1899).

The psychical disorders due to thyroid insufficiency may be associated with the following: infantilism, physical and mental backwardness, Hertoghe's chronic hypothyroidal syndrome, hypothyroidal temperament, hypothyroidal neurasthenia. Laignel-Lavastine (Le bulletin médical, Aug. 5, 1908).

Case of insanity in a myxedematous woman who was given for a week tablets prepared from the thyroid of the sheep. At the end of that brief period she was transformed from a stupid object into a bright and pleasant featured woman, quite unrecognizable as the creature of a week before.

Second case of insanity due to an excess of the thyroid secretion in the blood, manifested by great nervousness and excitability and many other symptoms, such as palpitation; there is a theory, not yet established, that excess of thyroid secretion is neutralized by some substance in the blood, of which substance (according to theory) there was not sufficient to neutralize the great excess; the patient was, therefore, supplied with serum (suprarenal extract?) from a goat whose thyroid had been removed. Apparently as a result of this treatment a good recovery was made. S. M. Robertson (Medical Times, August, 1911).

Such being the case, we can only expect benefit when increased metabolism and cell nutrition is required, *i.e.*, in **stuporous melancholias** due to defective nutrition, depressive states in general, when organic lesions are not present. Again, in view of the property thyroid preparations possess of promoting the proteolysis or breaking down of waste products we should expect benefit in **puerperal** and **climacteric insanities**. Clinical observation has sustained this interpretation. As a rule, however, psychiatrists have used entirely too large doses; hence, the untoward effects recorded.

Trial of thyroid in 130 patients whose insanity was definitely making no progress toward recovery under the methods adopted in the asylum, or whose insanity was becoming chronic or incurable. Each patient was put to bed during the period of experiment, and was given a staple diet sufficient to maintain body weight at its usual level, the administration of the extract beginning on the fifth day. The patient was weighed weekly during treatment and for a month after. The urine was regularly examined, and the urea was estimated by the hypobromite method. The phosphates in the urine were determined by the uranium method. The thyroid extract was administered in 130 cases of insanity (45 males and 85 females) with the following results: Where large doses were given there followed pyrexia in most of the cases to a slight or moderate degree. Loss of weight was a constant symptom; also increased sweating, pains and tinglings in various parts of the body, and a slight or moderate degree of exaltation, or restlessness. There was tachycardia in most cases, and the respirations were increased by about six per minute. Appetite and thirst increased, and in females menstruation was made more profuse than usual. Urea and nitrogenous products were increased in the urine, showing an enhanced metabolic activity. Slight transitory albuminuria was found in 10 per cent. of the cases. In moderate and small doses the above results were present in a correspondingly less degree, and it was concluded that the thyroid extract acted as a powerful metabolic (catabolic) stimulant. The patients included 5 idiots and imbeciles, 7 pubescent or adolescent cases, and cases of mania, melan-

cholia, myxedema, alcoholic and general paralytic insanity, etc. Of a total of 130 patients, 12 recovered, 29 were improved, and 89 were unimproved. The recoveries included 4 cases of **stupor**, 3 of **puerperal mania**, 1 of **lactational melancholia**, 1 of **myxedema**, 1 of simple melancholia, and 2 of **climacteric melancholia**. These patients also improved physically. The threatened attacks of **folie circulaire** were aborted by thyroid administration. C. C. Easterbrook (Lancet, Aug. 25, 1900).

Twenty-two patients treated with thyroid extract, administered in the form of 5-grain tablets. The dose was gradually increased from 10 grains daily to as much as 60 grains in some severe and otherwise intractable cases, and continued until reaction occurred. In all cases the patients were confined to bed during treatment, were most carefully nursed, and constant observations of pulse and temperature recorded. The treatment was discontinued when a noticeable rise of temperature or increased pulse rate was produced. In no case has the writer had any accident or reason to suspect that the patient was unfavorably influenced by the treatment. In 1 case, which he considered from the first a rather unfavorable one for treatment, a severe gastric crisis seemed to have resulted from the administration of the substances. This was the case of a girl with a neurotic inheritance who was partially demented and suffered from a large goiter. The treatment entirely removed the large goiter, but failed to produce any change in the mental state.

Of 22 cases treated suffering from various forms of mental trouble, 7 were males and 15 females. Three of the men completely recovered, and 2 of these 3 patients were homicidal to a marked degree.

The author has treated 3 patients in all suffering from **homicidal impulses** with thyroid extract. In all of these 3 cases a marked change took place subsequent to the thyroid treatment, and the morbid impulses seemed to be lost.

Of the 22 patients treated by the author with sheep's thyroid, 12 recovered and were discharged from the hospital, and have not since, so far as he can ascertain, been treated, with one exception, elsewhere or required readmission to St. Patrick's Hospital. Leeper (Med. Press and Circular, July 5, 1905).

Two cases of **dementia præcox** treated with thyroid. The first case, which was of the hebephrenic type, was completely cured, while the second, in which catatonia prevailed, was only temporarily benefited, the treatment being stopped after recurrence of the dementia. The best results are to be expected in the hebephrenic type. Levison (Hospitalstidende, No. 36, 1909).

Case illustrating the use of thyroid extract in **violent dementia præcox.** The patient, aged 22, was always more or less violent. When unwell she was more violent and troublesome than usual, repeatedly asking for a knife to cut her throat. The habits were very dirty, everything being passed in bed. She was very troublesome with food, having to be spoon-fed.

On January 19th the treatment by thyroid tabloids (5 grains in each) was begun. The intention was to increase the number of tabloids till such time as the pulse showed that it would be dangerous to give more, then suddenly to cease, and thus produce a crisis—the method usually adopted in such cases.

On the 19th 3 tabloids were given, and the number increased. When six tabloids a day were given, the patient began to get more restless and troublesome, and had to have special attention to prevent her getting into harm's way. The pulse, at first 80, had now risen to 100. The restless condition increased as the number of tabloids increased till the 6th of February, when she was having 11 a day. The pulse was 132, very compressible, but regular. She now began to speak sensibly, to take more interest in her surroundings, to have more control over her conduct, lying quietly in bed, and to become

cleaner in her habits. On the 10th the pulse was 150, the number of tabloids 12, and the mental condition was improving. The thyroid was then gradually reduced. The number of tabloids was maintained at 12 for some days, then gradually decreased with steady improvement in the mental state, except at 5, when the patient became very restless and sleepless. Sulphonal, gr. 15, was given on three successive nights, with good results, and she again continued to improve. On the 1st of March she was able to get out of bed for a few hours, but great care had to be taken to prevent any undue exertion. She got gradually stronger, and was able to go to the country on the 10th of March. She was then taking 1 tabloid a day, but this has now ceased. The pulse when she left was still about 120, but was of fair strength. No inconvenience was caused, though she had to be prevented from unduly exerting herself. The pulse has now come down to nearly normal. The mental improvement has continued, and she is now very bright, has lost all her shyness and dread of strangers, has taken up her music and painting, and is more her natural self than she has been for some time. A. Davidson (Austral. Med. Gaz., April 20, 1911).

Lactation.—Thyroid preparations have been recommended as galactagogues by Hertoghe, Chéron, and others. In some cases on record the secretion of milk was free as long as thyroid was taken and failed as soon as it was neglected. This is obviously due to its stimulating influence on general oxidation, all functions being enhanced.

The value of the administration of thyroid as a means of increasing the activity of the mammary glands had already been demonstrated by Hertoghe in 1900 in patients presenting mild symptoms of thyroid insufficiency. The writer confirms the latter's observations, but believes that the period of lactation is not the best time during which to begin the thyroid medication. He has obtained better results by beginning the treatment in the early months of pregnancy, during the time when the mammary glands are transforming from a state of rest to one of activity. This therapeutic measure is recommended particularly in women who have already given evidence of inability to nurse their children wholly or in part. The dose of thyroid administered is about 0.1 Gm. (1½ grains) from one to three times a day. The result of this treatment is a copious secretion of milk after the birth of the child. A. Siegmund (Zentralbl. f. Gynäk., Oct. 15 and 22, 1910).

Middle-ear Disorders. — Thyroid preparations have been tried in several of these disorders, sclerosis, middle-ear catarrh, ossicular sclerosis, etc., but the results, on the whole, were not encouraging. They should be tried, however, in suppurative processes associated with general adynamia, as these often persist merely because the bactericidal and antitoxic powers of the blood are deficient. Thyroid, by enhancing these protective functions, has at least proven valuable in ulcerative disorders located elsewhere, even when osseous tissue was involved, as in osteomyelitis.

Nervous Disorders. — Epilepsy. — This disease is sometimes greatly benefited by the use of thyroid preparations, but only when small doses are used. Untoward results are readily caused by excessive dosage, as shown by loss of weight. Coincidently, meat should be removed from the diet, and the patient ordered to drink copiously of water. The spasmogenic wastes are thus increasingly broken down by the thyroid; they are formed less freely owing to the abstraction of meat, and the end products of metabolism are more readily eliminated by the kidneys owing to the free use of water. I have observed excellent results through this treatment. It must not be forgot-

ten, however, that other factors—intestinal worms, indigestible foods, scars, dentition, alcohol, lead poisoning, syphilis, nasal growths, dental interpressure, and phimoses—may produce epilepsy, and that the cause must be removed in such cases if a satisfactory result is to be obtained.

Case of **epileptic idiocy** with diffuse lipomata, ichthyosis, and nevi successfully treated with thyroid extract. In this typical case, the thyroid extract supplied the exact want; the ichthyosis almost disappeared, the lipomata decreased in size, and the intelligence of the boy improved. Whether or not the congenital absence of the thyroid gland is the primary cause of all his symptoms is at present difficult to say, although the marked improvement strongly points in that direction. Nathan Raw (Jour. of Mental Sci., Oct., 1897).

In the young there occurs a class of cases characterized by recurrent attacks of a heterogeneous type, that may conveniently be called **"pseudoepilepsy."** This form is curable. Such cases, so far as here studied, are due to, or associated with, disturbances in the general tissue metabolism of the body. Some of these are in whole or in part of rachitic origin. Troubles of this kind when due to rachitis are amenable to thyroid treatment. True epilepsy is not remedied by thyroid, even in a person who was once rachitic. It is evident that in many cases there is a closer relationship between rachitis and athyrosis than has heretofore been recognized. There must be a relative inadequacy of the thyroid function in those cases associated with rickets. Either, as one of the author's cases indicates, there is a serious impairment of the activity of the gland or thyroid feeding serves to burn up harmful material at large in the system. William Browning (Jour. Nerv. and Mental Dis., Oct., 1902).

Case of a man aged 20 who began to suffer from **epileptic fits** and simultaneously enlargement of the thyroid gland. Two years of bromide had no effect. Treatment of the thyroid with electricity and iodine brought about a reduction in size of the thyroid and complete cessation of fits. The positive electrode was wrapped in wool, soaked in iodine, and applied to the gland. Other writers have proved that there is a definite relationship between epilepsy and the thyroid, and this is supported by experiments on animals. Crisafulli (Il Morgagni, April, 1903).

A conclusion forces itself upon us, viz., that idiopathic **epilepsy** is always associated with defective metabolic processes. The latter may originate from many sources. There is a certain class of epileptics whose seizures are in direct relationship with a disturbed function of the ductless glands and particularly the thyroid. In such cases the reason for failure of the usual treatment lies in the want of thyroid feeding. Administration of the latter will be of great benefit. Six illustrative cases. Alfred Gordon (Penna. Med. Jour., July, 1908).

Three cases of **epilepsy** in which the simplifying influence of Dr. Sajous's discoveries as to the functions of the ductless glands and other body structures is clearly shown by good results. All three being due to the retention of excrementitious substances in the blood, and the irritating action of these poisons upon the spasmogenic centers—the indications, of course, were to destroy these poisons. Drugs known to do so by increasing the antitoxic substances through the ductless glands—mercury and desiccated thyroid—were administered. To assist this antitoxic process of the osmotic properties of the blood, physiological saline solution was given as beverage. On the other hand, the sources of intoxication were as much as possible eliminated by purgation and dietetic measures calculated to prevent the accumulation in the blood-stream of any toxic wastes, *i.e.*, wastes imperfectly prepared for prompt elimination by the kidneys. J. Madison Taylor (Monthly Cyclo. of Pract. Med., March, 1909).

When **epilepsy** is complicated by **bromism** this may be combated with

thyroid gland. A cachet 0.1 Gm. (1½ grains) of desiccated thyroid is given every morning for three weeks, then suspended from time to time for a fortnight. Two doses, each of 1 Gm. (15 grains) of potassium bromide, are given daily at equal intervals, say at 10 A.M. and 10 P.M., apart from meals, and dissolved in half a wineglassful or less of water. The bromide is to be given regularly without suspending the treatment. J. A. Sicard (Jour. de méd. de Paris, Nov. 19, 1910).

The writer emphasizes the following points: The undeniable relation of **epileptic seizures** to menstruation. Absolute freedom from attacks in the intervals between menstrual periods. Apparently perfect integrity of the ovaries and still occurrence of epileptic fits immediately before or during menstruation. The inability of controlling the fits with the usual bromide treatment. The good and even excellent effect of thyroid extract. The mode of administration of the latter, viz., thyroid extract between the menstrual periods and bromides without thyroid only a few days before menstruation. Alfred Gordon (Penna. Med. Jour., Feb., 1910).

Two **cases** of **cretinism** in twin brothers, both of whom suffered in addition, one from **epileptic seizures,** the other from a marked degree of **ataxia.** The epileptic attacks began at the age of 23 and rapidly increased in frequency until they were of almost daily occurrence; there were occasional attacks of *petit mal* besides the seizures of *grand mal.* The attacks were greatly modified by thyroid therapy, although this patient could not tolerate more than 25 grains of the extract daily. The other twin, when 14 years old, developed a staggering gait, walking like a drunken man, and suffering severe pains about the hips; the arms soon became involved so that he could hardly write. This patient began by taking 15 grains of thyroid extract a day, and the dose was increased gradually until he was taking 45 grains a day without toxic manifestations. All his symptoms improved, including the ataxia; he is able to walk (though with a waddling movement) and to write, earning his living by typewriting. L. S. Manson (Med. Record, Jan. 1, 1910).

Eclampsia.—It is now generally recognized that this complication of the puerperal state is due to toxemia. Thyroid extract is indicated, therefore, since it enhances the destruction of toxic wastes and other poisons.

This accounts, from my viewpoint, for the fact that a number of cases have been reported in which the convulsions ceased under the influence of rather large doses of thyroid gland. Nicholson obtained excellent results with 7½ grains of thyroid extract every three or four hours, with morphine as an adjunct. Baldowsky confirmed its value in 2 cases; in the first, a multipara in the seventh month of pregnancy, a convulsion occurring, 18 grains of thyroid extract were given. The fits ceased. The thyroid was continued for two days longer—10 grains daily—and the patient seemed quite recovered. A fortnight later she again developed severe eclamptic fits, sixteen seizures altogether, which were treated by thyroid extract, with narcotic remedies, and recovery followed. The other was a primipara at term who was suddenly seized with convulsions at the commencement of labor. Thyroid extract alone was given, and the attack ceased before the rupture of the membranes. The labor took place without any unusual symptom, and the puerperium was normal.

I have pointed out, however, that the action of the thyroid is greatly enhanced by the simultaneous use of hypodermoclysis. In some cases the thyroid preparation was dissolved in the saline solution injected.

Severe case in which, 2 pints of saline solution having been prepared, 15 tabloids of extract of thyroid (5 grains each, B. W. & Co.) were dissolved in the saline and injected below the breast. Within an hour and a half there was a decided improvement, both in the frequency and severity of the fits, and in another hour the bowels moved and labor began. Under chloroform the labor was terminated with forceps with as little delay as possible, and on the removal of the placenta bleeding was freely encouraged. The child was dead. The fits numbered 37, so far as could be counted. From this time onward the fits ceased. She remained semiconscious for forty-eight hours, when she developed a right basal pneumonia, with a crisis seven days later, after which she made a rapid recovery. The urine was examined three weeks afterward, and found to contain only a trace of albumin. J. C. G. Macnab and D. S. E. Macnab (Jour. of Obstet. and Gyn., Nov., 1904).

Migraine.—This disorder is now generally attributed to the gouty diathesis, *i.e.*, to the accumulation in the blood of intermediate waste products of the purin or alloxuric type. Thyroid preparations, by promoting the conversion of these toxic products into bodies that are readily eliminated by the kidneys, antagonize this pathogenic process. But here, again, small doses are alone indicated; 1 or 2 grains (0.6 to 0.13 Gm.) of desiccated thyroid during meals suffice at first, the effect being kept up after a few weeks by a single grain daily. The free use of water as beverage, abstention from red meats, and out-of-door exercise are necessary accompaniments to obtain the best results.

Case of very severe recurrent **migraine** in which the writer used thyroid extract with success. The patient was a woman aged 40 years who since childhood had been subject to extremely severe hemicranias, accompanied by injection and irritation of the conjunctiva of the eye on the corresponding side, a dilatation of the pupil, and blepharospasm. The attacks of migraine in this case recurred with great regularity about every twenty-eight days and usually preceded the menstrual periods. The correspondence of the menstruation and the migraine in this case was very complete. The woman had no attacks of migraine during pregnancy and lactation, but developed the same attacks after weaning her infant. At the age of 36 years, her flow became irregular and the attacks followed suit. It was then that thyroid treatment was thought of. The theoretical basis for this treatment in such cases is that the attacks of migraine are caused through vasomotor changes induced by the circulation of certain toxins in the body, which are derived from an insufficiency in the function of the thyroid gland, or from a disturbance in the balance of internal secretion between the gland and the ovaries. Tablets of thyroid extract were, therefore, given to this patient, with the result that within two months not only was the menstrual function restored to regularity, but the attacks of migraine totally disappeared. Consiglio (Gaz. degli Ospedali, Nov. 20, 1904).

Certain obstinate forms of **headache** are due to thyroid deficiency. Such patients may be relieved by thyroid tablets. In every **migraine** of unknown origin, inquiry should be made into the functions of the thyroid and for the presence of symptoms of hypothyroidism. If these signs are present, thyroid medication should be resorted to.

Thyroid migraine does not differ in its signs from common migraine. It is either precocious or tardy, hereditary or acquired, uni- or bi- lateral, or it may be syndromic or symptomatic. It may last only some hours or some days, but it is always paroxysmic. Cephalalgia accompanied by vomiting requires rest and quiet in bed. It may depend upon some ophthalmic trouble. Other varieties of **cephalalgia** are also favorably influenced by thyroid treatment.

Léopold-Lévi and de Rothschild (Bull. et mém. de la Soc. Méd. des Hôpitaux de Paris, May 17, 1906).

Case of **autointoxication** of intestinal origin manifested by violent **migraine.** When the colon bacilli were isolated it was found that 5 c.c. injected into a rat killed it in a few hours. This is a very marked degree of virulency, for it is sometimes possible to inject as high as 10 c.c. without effect. No treatment proving curative and his skin being dry, he was given thyroid gland, beginning with 1 grain, increased to 2 three times a day. Within two weeks the symptoms all disappeared. At the end of two months the writer again injected the *Bacillus coli* into a rat, and it had lost its virulency. That was a year ago, and he has had no recurrence. The writer had another case which presented this marked symptom of dry skin and headache. This patient also suffered from double vision. The writer examined the feces and found a very high virulency of the *Bacillus coli.* Began treatment with the thyroid substance, and the case showed that the bacilli were no longer virulent. F. B. Turck (Jour. Med. Soc. of New Jersey, July, 1911).

Asthma.—A certain proportion of these cases is also, as is well known, a manifestation of the gouty diathesis. Hence, the value of thyroid preparations owing to the antitoxic action which renders them useful in migraine.

A certain percentage of cases of **asthma,** in particular those of the essential or "neuroarthritic" type, is favorably influenced by the use of thyroid or corpus luteum preparations. The experience of the authors with this mode of treatment amounts to 14 cases, of which 7 (50 per cent.) were notably benefited. Thyroid was used in 6 of these patients, corpus luteum in 1.

The use of thyroid in small doses may cause improvement in certain cases of **pseudoasthma** associated with emphysema, certain instances of dyspnea of asthmatic type (in renal and gastric infections), or of paroxysmal type (in pulmonary sclerosis of tuberculous origin), as well as in cases of ordinary **"nasal asthma,"** or even **"hay asthma."** Léopold-Lévi and H. de Rothschild (Bull. méd., May 14, 1910).

Tetanus.—As thyroid preparations promptly arrest the tetanus that occurs after removal of the thyroid, they suggest themselves not only as prophylactics, but also to assist tetanus antitoxin. The latter sometimes fails merely because the spasmogenic poisons are not sensitized or "opsonized" to its effects, as shown by a comparatively low temperature; desiccated thyroid in full doses tends to correct this condition and to increase the chances of recovery.

Osseous Disorders.—As far back as 1897 Gabriel Gauthier showed that **delayed union in fractures** was counteracted by thyroid preparations, consolidation occurring in some instances as early as the fifteenth day. Similar results have been obtained by many observers, the proportion of successful cases being about 60 per cent. Removal of the thyroid had been found by Hanan, Steinlein, and Bayon to prevent the healing of fractures in otherwise healthy animals, thus affording a sound basis for the use of thyroid preparations. Its beneficial effects are best shown in the young, its value decreasing as the patient is more advanced.

The absence of this gland materially affects the normal healing of a fracture. There is a delay in the development of both the callus and the following retrogressive metamorphosis. For the first two weeks no difference microscopically could be seen, but by three weeks the fracture in the normal animal was almost completely ossified, whereas in the animal from whom the thyroid

gland had been removed the callus consisted almost entirely of pure cartilage. Even after eleven weeks there was still some cartilage present around the fracture in those animals which had had their thyroids removed, but complete ossification did finally take place. The formation of the new medullary canal began during the eleventh week, but was not completed twenty-four weeks after the fracture. The callus in the animals deprived of the thyroid gland is smaller than in normal animals during the stage of development, but during the stages of retrograde metamorphosis it is larger than normal. The difference in the healing of fractures between normal animals and those deprived of their thyroids is greater the longer the time since the removal of the gland to the time of fracture. Steinlein (Archiv f. klin. Chir., Bd. 60, H. 2, 1900).

Thyroid preparations have also been used with success in **osteomalacia, rickets,** and **osteomyelitis.** All these beneficial effects are explained by the influence of thyroid on metabolism, all functions, including the processes of repair, being enhanced. The marked influence of the thyroid over calcium metabolism shown by Parhon, Macallum, and others is another potent factor in the marked benefit noted in these disorders.

In 5 cases of **rachitis** the effects of thyroid were marked, the children rapidly increasing in height under the influence of the mild organotherapy, and without displaying any evidence of intolerance. They seemed to benefit in every way by the thyroid treatment, becoming more intelligent and lively during the two weeks' and six weeks' courses with an interval of two months. Variot and Pironneau (Bull. de la Soc. de Ped., April, 1911).

Rheumatism, Chronic Progressive.—Following the experience of Revilliod, Lancereaux has urged the value of thyroid preparations in this class of disorders many years, but, as is often the case, the scoffers of the profession have caused the valuable observations of both these distinguished clinicians to be ignored, thus perpetuating needlessly the acute sufferings of the many victims of this disease. When its pathogenesis is interpreted from my standpoint (see "Internal Secretions" Suppl., p. 1869, 1907), *i.e.*, "inadequate catabolism of tissue wastes and excitation by the toxic products formed of the vasomotor center," the favorable influence of thyroid preparations is self-evident: the toxic wastes which provoke excessive vascular tension and pain being more actively broken down, the primary cause of the disorder is removed. Souques (1908), in 2 cases of this disease, found the thyroid gland atrophied. Many cases have recently been treated successfully. Léopold-Lévi and de Rothschild, who have had the greatest experience with this class of cases, recommend—in keeping with the teachings of my own experience, and now sustained by the experience of many other clinicians—that small doses should be used.

[As Rachford (Phila. Med. Jour., April 16, 1898) observed nine years ago, "thyroid feeding will increase the excretion of the alloxuric bodies in the urine, and will produce an acute arthritis in a patient suffering from chronic rheumatic gout." Large doses will thus prove harmful where small doses will prove beneficial. C. E. DE M. S.]

Case of a man who had suffered for thirty-six years from **rheumatism** and **gout,** with decided arteriosclerosis, high-tension pulse, heart hypertrophied, and albuminuria, who under the influence of Baumann's iodothyrin, started with ½ Gm. daily—increasing ⅙ Gm.—was relieved of the pain in the limbs, polyuria and albuminuria controlled, the heart improved, tension of the pulse lessened, although it was more rapid. Lance-

reaux and Paulesco (Bulletin de l'Acad. de Méd., Jan. 3, 1899).

In **acute rheumatic fever** there are usually swelling and tenderness of the thyroid, usually running parallel with the general disease, and experience has shown that if the swelling and tenderness of the thyroid diminishes without a similar improvement in the general condition the attack is likely to be an obstinate one, and if the thyroid symptoms fail to appear at all treatment is likely to be unsatisfactory, while a parallelism between thyroid involvement and the joint disease suggests a favorable prognosis. The thyroid secretion is antibacterial in action and supports the organism in its effort to overcome the disease. The direct action of the iodine preparations on the thyroid may explain their therapeutic value in the treatment of rheumatism. Vincent (Bull. et mém. de la Soc. Méd. des Hôp., No. 14, 1907).

Case of a young woman 28 years of age who was being treated by X-rays for hypertrichosis of the chin. She was free from any known hereditary influence. After the second *séance* she noted pains in the ankles and toes; after the eighteenth *séance* of the Roentgen rays the **rheumatic manifestations** extended to the right knee and to the hands. At the same time her face became puffy in appearance, and she became physically and mentally apathetic. On examination painful tumefaction of the ankles and toes was found, and very marked swellings of the joints of the right hand and fingers, accompanied by edema, were present. The visceral functions were normal, although there were dyspeptic disturbances and menstruation was excessive. The thyroid gland was found to be markedly diminished in volume.

The ordinary antirheumatic treatment proved of no value, and, struck by the thyroid alterations, the mental change, the puffiness, etc., the author was led to the use of thyroid medication. Two-grain tablets of the desiccated gland were first employed. Four days after thyroid medication was begun the articular pains ceased, the swellings went down, and in three weeks the patient was able to take up her ordinary occupations. M. Acchioté (Gazette Méd. d'Orient, May, 1907).

Report of 39 cases of **chronic rheumatism** during the last three years in which treatment was with desiccated and pulverized sheep thyroids; from 1 to 3 doses a day of 10 cg. each, equivalent to 50 cg. of fresh glands, were given. The patients' ages ranged from 12 to 75 years, and in 5 cases the deformity resulting from the rheumatism had confined the patients to bed for years. In 9 other cases the persistence of the pains, recurrence of subacute attacks, and deformities were very distressing. In 19 grave or severe cases, 2 of the patients can now be regarded as clinically cured under the treatment, and in 14 cases there was great improvement either in the pain, the functional impotence or the deformity in the joints or elsewhere. In 20 moderate or mild cases of chronic rheumatism, 18 of the patients were immeasurably improved or cured. The results were better the more recent and milder the cases. The benefit has persisted in the various cases. Léopold-Lévi and de Rothschild (Bull. de l'Acad. de Méd., March 10, 1908).

Uterine Disorders.—Various conditions of the genital apparatus, such as the onset of **puberty, pregnancy, fibroid tumor,** which cause a distinct change in the metabolism of the entire organism, frequently produce enlargement of the thyroid gland. Again, the deficiency of the normal thyroid secretion following thyroidectomy in myxedema, cretinism, etc., is often associated with atrophic changes in the genital apparatus, as shown by Fisher, of Vienna.

This clearly indicates direct association between the thyroid and the genital system, and has suggested the use of thyroid preparations. The **vomiting of pregnancy** is also benefited by their use.

Five cases of **pernicious nausea of pregnancy** in which the writer has had good results by the administration of thyroidin. Four of these cases were under his immediate observation, and 1 was treated by a colleague. The remedy is administered several hours before the time when the worst paroxysms of vomiting appear. The stomach must be absolutely empty at the time of the administration. It is usually best to give it in the early morning before the patient leaves her bed. She is encouraged to sleep afterward and to take nourishment before getting up. From an hour to half an hour, however, before the other meals of the day, the remedy should be used, and also before going to bed. The morning dose should be the largest, 6 decigrams being given in some cases. If the patient vomits in the evening, a similar dose should be given before this time. The remedy is best used in powder, and sometimes sodium bicarbonate or bismuth may be combined with it to advantage. Siegmund (Zentralbl. f. Gynäk., Nu. 42, 1910).

They have been found of value for the purpose of arresting **hemorrhage**, whether this occur in connection with **abortion**, tumors, or **uterine malpositions**. A remarkable case of **metrorrhagia** due to hemophilia successfully treated with thyroid extract was reported by Déjace. In the disorders of **menopause**, hemorrhages, flushes, irritability, migraine, etc., thyroid preparations are of undoubted value owing to their ability to promote the destruction of waste products, which underlie these morbid phenomena.

It is very probable that the toxemia of pregnancy is largely dependent upon faulty metabolism; at least, an insufficient metabolism is an accompaniment which greatly adds to the seriousness of the condition. Failure of the thyroid gland to hypertrophy during pregnancy is probably followed by insufficient metabolism, and may result in the various forms of toxemia of pregnancy. When there is a failure of the normal hypertrophy of the thyroid gland during pregnancy and when there is a diseased thyroid, as in Graves's disease, the administration of thyroid substance, by supplying the deficiency of the normal thyroid secretion and by diuretic action, may materially improve a faulty metabolism and thus give a favorable influence upon the manifestations of the **toxemia of pregnancy**. Ward (Surg., Gynec., and Obstet., Dec., 1909).

Summary.—Thyroid preparations have been used and recommended in many other diseases, but the foregoing seem to me to represent those in which they are productive of real good. My own experience has suggested that this would prove true, particularly as to desiccated thyroid:—

1. In diseases due to slowed destruction of toxic wastes, as shown by its action in **tetany, epilepsy, eclampsia, disorders of menopause, asthma, chronic rheumatism, migraine**, and also by those due to slow oxidation of fats, as in **obesity** and **Dercum's disease: adiposis dolorosa.**

2. In diseases due to lowered general nutrition of all tissues, including the bones, as shown by its action in **cretinism, myxedema**, and kindred disorders—**osteomalacia, rickets**, and **osteomyelitis.**

3. In disorders due to lowered nutrition of the muscular elements, including the skeletal and vascular muscles, as shown by its action in **general adynamia, neurasthenia**, and **myasthenia.**

4. In all cases in which the processes of repair or absorption are deficient, as shown by its action in **delayed union of fractures, certain benign and malignant neoplasms**, and **syphilitic tissue and bone necrosis.**

5. In infectious diseases—owing to the increase of autoantitoxin, thyro-

iodase (opsonin), and phagocytes—as shown by its action in **tuberculosis, typhoid fever, infectious tonsillitis, certain exanthemata,** and, in general, **infections** in which fever is a prominent symptom.

PARATHYROID ORGANOTHERAPY.

The two internal of these four small glandules were described, as previously stated, by Sandström in 1880, while the two external were discovered by Nicholas in 1893, and also in 1895 by Kohn. Though distinct from the thyroid gland, they are in close apposition to, and sometimes imbedded in, this organ, and are supplied mainly by the inferior thyroid artery. Though histologically different from the thyroid gland, they also contain a colloid substance in which iodine occurs in relatively large proportion. That they carry on some general function is shown by the fact that their removal causes tetany, while removal of the thyroid divested of its parathyroids causes myxedema, arrests growth, and impairs calcium metabolism, the bones, including the teeth, becoming soft and brittle.

When the extirpation of all the parathyroid glands is complete, tetany appears, even in herbivora. Failure to produce tetany experimentally is probably due to the fact that some parathyroid tissue remains. Only a very small amount of parathyroid tissue is required to prevent tetany. The experiments of the writers suggest that calcium salts have a moderating influence upon the nerve-cells. The parathyroid secretion in some way controls the calcium exchange in the body. In tetany there is a marked reduction in a calcium content of the tissues and an increased output in the urine and feces. The injection of a solution of a salt of calcium into the circulation of an animal in tetany promptly checks all the symptoms; the injection of sodium or potassium salts tends to intensify the symptoms. The effect of magnesium salts is marked by its toxic action. The relief by calcium is temporary. The same relief is obtained by the injection of an emulsion of parathyroid glands. Often the temporary relief is sufficient, as the remnants of parathyroid tissue may recover their function. MacCallum and Voegtlin (Jour. of Exper. Med., Jan. 9, 1909).

Experiments upon animals have suggested that the parathyroids play an indisputable rôle in osteogenesis; that their action is equally distinct in the growth of healthy bone, and the cicatrization of fractured bone; that their action, which is certain on the young organism, seems to be *nil* upon adults; that all or part of the rôle in osteogenesis attributed to the thyroid should be assigned to the parathyroids, and that it would be important to make a trial in man of the accelerating action of parathyroid medication in the consolidation of fractures in the young. Morel (Archiv gén. d. chir., vol. vi, p. 231, 1910).

Confirmation of the relationship between the parathyroids and calcium metabolism. In rodents the incisor teeth undergo constant growth. During experiments on the relationship between parathyroid extirpation and tetany, the writer noticed that the incisor teeth of the rats became repeatedly fractured. He found that in the normal incisor tooth of this animal the dentin forms the principal portion; a conical pulp cavity pierces this longitudinally, and a narrow zone of dentin adjoining this cavity normally undergoes calcification, while the greater part has already received its complete deposit of calcium. On removal of the parathyroids, it was found that calcification of the dentin at once ceased more or less completely; the portion already hardened underwent no change, but as the effects of use wore down this older part the new uncalcified dentin taking its place lacked strength, and fractures followed.

Imperfections in the enamel deposit also occurred, though at a later period than the alterations in the dentin. By regulating the time between extirpation of the glands and examination of the tooth, all transitional stages between the normal tooth and one almost completely decalcified could be obtained.

Again, transplantation of the parathyroids from the neck to the abdominal wall was successfully accomplished in 9 cases. In each instance there was found in the incisor teeth a zone of uncalcified dentin, corresponding to the period of parathyroid quiescence, interposed between two layers of normal dentin. This demonstrates clearly the influence of the parathyroids on calcium metabolism. Erdheim (Zeitsch. f. Pathol., Bd. vii, S. 178, 1911).

The functions of the parathyroids are still in doubt; some investigators claim that they have no independent function; others that they govern calcium metabolism independently of the thyroid. A third group, to which my own researches have caused me to belong, believe that they supply a secretion which combines with that of the thyroid to carry on the functions of the latter, *i.e.*, to sustain tissue and calcium metabolism besides carrying on their antitoxic functions. From my viewpoint, their secretion plays the principal rôle in the formation of Wright's opsonin in conjunction with the thyroid, as shown under the preceding heading.

[The investigations of King, Biondi (Berl. klin. Woch., xxv, p. 954, 1888), Zielinska (Virchow's Archiv, cxxxvi, p. 170, 1894), Vassale and de Brazza (Arch. ital. di biologia, xxiii, p. 292, 1895) on the thyroid, and those of Welsh (Jour. of Anat. and Physiol., April, 1898), and Capobianco and Mazziato (Giorn. Int. de Scienze, Nos. 8, 9, and 10, 1899), and others on the parathyroids, have shown that the product of these organs passes into perivascular lymph-spaces. Being then transferred to the larger cervical lymphatics, they are discharged by the right and left lymphatic ducts—the thoracic duct, according to Pembrey (Hill's "Recent Advances in Physiology," p. 579)—into the subclavian veins, and by way of the superior vena cava to the heart. Here they become merged with the venous blood of the entire organism, forming a single secretion—in accord with Gley's (La Presse médicale, January 12, 1898) view—which is then inevitably carried to the heart, and thence to the lungs. As the venous blood carrying the secretion passes to these organs to be oxygenized, the secretion itself is likewise carried to the air-cells.

The purpose of this itinerary suggests itself when we recall that, as stated by Nothnagel and Rossbach (Thérapeutique, p. 261, 1889), hemoglobin can fix large quantities of iodine. It accounts also for the fact that Gley (La Semaine médicale, May 25, 1898) and Bourcet found iodine in the red corpuscles. Being a component of the albuminous hemoglobin of these cells with adrenoxidase, however, iodine should be found in all tissues. While Bourcet (cited by Morat and Doyon, Traité de physiologie, vol. i, p. 470, 1904) ascertained that such was the case, Justus (Virchow's Archiv, clxxvi, p. 1, 1904) found it in all cellular nuclei. This latter feature is important, since, as we have seen, iodine serves to increase the inflammability, as it were, of the phosphorus which all nuclei contain. C. E. DE M. S.]

THERAPEUTICS.—The actual value of parathyroid in therapeutics has not as yet been clearly determined. It has been tried with benefit in **postoperative tetany** by several clinicians. MacCallum found large quantities injected intravenously necessary. Vassale, James, and Halsted have also had favorable results. While Birch found thyroid ineffectual, parathyroid caused recovery.

The nucleoproteid of the parathyroid relieves the symptoms of acute tetany in dogs, but the globulin has no such power. Boiling or heating the nucleoproteid solution at 80° C. for half an hour destroys its activity, and it de-

teriorates rapidly when kept in solution or frozen. The nucleoproteid relieves tetany by the mouth, but more effectively when given subcutaneously or intraperitoneally. Berkeley and Beebe (Jour. Med. Research, Feb., 1909).

Three cases found in literature and 1 personal case in which the transplantation of human parathyroids was followed by recovery. Danielson (Beiträge z. klin. Chir., Bd. xxxvii, S. 998, 1910).

In **postoperative parathyroid tetany** —which is prevented by removing only, as does Kocher, the central part of the thyroid, thus leaving intact the posterior capsule, to which the parathyroids adhere—the spasms may be arrested by implanting human thyroids from persons who have just died of some non-infectious disease. Implanted glands do not act at once; it is only when they assume their normal functions *in situ* that recovery occurs.

Study undertaken with a view to determine the course to be pursued by the surgeon when a parathyroid gland has been accidentally removed or deprived of its blood supply, and in the hope that it might be attended with such success as to justify the attempt to transplant this glandule from man to man. The transplantations were made either into the thyroid, the spleen, or in or behind the rectus muscle of the abdomen, and were both auto- and iso- transplantations. The writer's deductions were as follows:—

1. The autotransplantation of parathyroid glandules into the thyroid gland and behind the musculus rectus abdominis has been successful in 61 per cent. of the cases in which a deficiency greater than one-half has been created.

2. In no instance has the autotransplantation succeeded without the creation of such a deficiency.

3. Isotransplantation has been uniformly unsuccessful.

4. Parathyroid tissue transplanted in excess of what is urgently required by the organism has not lived.

5. One parathyroid autograft may suffice to maintain the animal in good health and spirits for many months and possibly for years.

6. Excised or deprived of their blood supply in the course of operation upon the human subject, parathyroid glands should, in the present state of our knowledge, be grafted, and probably into the thyroid gland.

7. Complete excision of the thyroid lobes in dogs may be well borne for a year or more. The myxedema, which usually has manifested itself within a few weeks, has not increased after the first few months. May it subsequently diminish with the hypertrophy of accessory thyroids?

8. Parathyroid tissue is essential to the life of dogs, as has been conclusively proven by the result of excision of the sole sustaining graft. W. S. Halsted (Jour. of Exper. Med., vol. xi, No. 1, 1909).

The indifference of some surgeons in respect to the importance of these parathyroids merits severe criticism. Personal case which, their advice being followed, developed very severe **tetany.** The case was saved, only after all other measures had been tried in vain, by the implantation of a thyroid, with its parathyroids, obtained from a small monkey and, one month later, of 3 parathyroids and a piece of thyroid the size of a small walnut, all obtained one-half hour after death from the body of a man who had died of Bright's disease and uremia. These tissues, placed at once in normal saline solution at 32° F. (0° C.), were implanted successfully within an hour, the simian thyroid beneath the patient's sternomastoid, and the human thyroid and parathyroid beneath her left rectus abdominis, under chloroform anesthesia. W. H. Brown (Annals of Surg., March, 1911).

An emulsion of fresh parathyroids may also arrest the spasms, but obviously only as long as the injected emulsion is active. It is administered in saline solution subcutaneously. It may

prove curative, as in the case cited below, but here the parathyroids were only partly removed, the recovery being eventually due to the resumption of function by the latter.

> Case treated successfully by means of an emulsion of parathyroids given subcutaneously. Five fresh beef parathyroids were placed in a 1:1000 solution of bichloride of mercury and allowed to soak about ten minutes. The glands were cut, under strict asepsis, into 5 pieces under physiological salt solution. These pieces were placed in a mortar and ground into a homogeneous mass, 400 c.c. of sterile salt solution being poured into the mortar. This was then filtered and given as salt transfusion into the patient's breast. The oral use of thyroid and parathyroid extract and the feeding of raw parathyroids had proved entirely useless. Only 1 parathyroid had been entirely removed, and the 3 others only partly so. Branham (Amer. Jour. Med. Sci., vol. xlviii, p. 161, 1908).

[In this case the injured parathyroids recovered and resumed their functions. The emulsion only served, therefore, to compensate for the temporary absence of secretion following the partial destruction of the three parathyroids and did not itself bring on recovery. C. E. DE M. S.]

Meat should not be given to such cases, since it increases the tetany. The diet should be limited to milk, farinaceous foods, and fruit. Exercise is harmful by promoting the formation of spasmogenic waste products. Rest in bed or in an armchair tends to reduce the frequency and violence of the spasms.

Vassale claims that the parathyroid extract relieves **eclampsia** as certainly as thyroid does myxedema, while Berkeley tried it with some degree of success in **paralysis agitans**. The latter gives 5 to 8 glands per day, minced and eaten in a bread-and-butter sandwich.

> The writer has treated in consultation and in his own practice 60 cases of **paralysis agitans** with parathyroid. Of these between 60 and 65 per cent. who have given the remedy a fair trial have spoken favorably of it and have continued the treatment. More than a dozen who began three or four years ago have greatly improved and are now only uncomfortable when they are without the medicine. The writer concludes that with such a percentage of benefited cases as this there seems no longer any reasonable doubt of the etiological relation between the disease and the remedy. One or 2 cases in the hands of medical friends or correspondents appear to be almost cured, though of such a disease in a patient of advancing years a "cure" is always to be spoken of with reserve. Berkeley (Med. Record, Dec. 24, 1910).

Simonine also speaks of encouraging results in **Sydenham's chorea** (5 cures), but the remedy has been tried by too few observers to warrant a conclusion as to its actual value.

ADRENAL OR SUPRARENAL ORGANOTHERAPY.

Brown-Séquard showed in 1856 that death followed removal of both adrenals in from a few hours to three days after a series of general phenomena corresponding to those of Addison's disease, viz., steady decline of the blood-pressure, intense prostration, and muscular weakness. This observation was not only confirmed by many other investigators, but Oliver and Schäfer, Szymonowicz, and Cybulski showed that adrenal extract caused a marked, though ephemeral rise of the blood-pressure and increased the power of the cardiac contractions. This was attributed to a direct action on the muscular elements of the arterioles and on the cardiac muscle, accompanied probably by excitation of the vasomotor center. The pulse- and heart- beats are

slowed, but strengthened. Gerhardt ascribes these phenomena to the rise of blood-pressure, Ambert to stimulation of the inhibitory center because division of the vagi arrests them. They are produced by a minute dose of the active principle when it is administered intravenously, but much larger doses have no effect when given by mouth or subcutaneously. Blum and others have found that adrenal extractives cause glycosuria, while Josué has shown that they provoke arteriosclerosis, an observation confirmed by many investigators.

The action of adrenal preparations is exercised upon involuntary muscles —those of the vessels, heart, intestines, and uterus, for example. But, according to the prevailing view, this action may be antagonistic; it may cause contraction of the intestinal vessels, for instance, but relax the muscular coats of the intestines. This has been ascribed by some to a direct action on the nerve-terminals; by others to a chemical action on the muscular elements. The secretory activity of the lachrymal and salivary glands is enhanced.

PHYSIOLOGICAL ACTION.—All these phenomena having remained unexplained, personal researches and a large number of experimental and clinical facts found in literature led me to the conclusion in 1903 that the physiological function of the adrenal secretion was (1) to take up the oxygen of the air in the pulmonary alveoli and carry this gas to the tissues as a constituent of the oxyhemoglobin, and (2) that it was the adrenal secretion which, as far as the rôle of oxygen in these processes is concerned, sustained oxidation and metabolism.

[Referring the reader to the article on "Adrenals, Diseases of," in this volume and to my work on the "Internal Secretions and the Principles of Medicine," the main factors determined by my investigations were briefly: (1) that the secretion of the adrenals has a marked affinity for oxygen, and that, owing to its passage into the inferior vena cava, it is inevitably carried to the pulmonary air-cells; (2) that once here it absorbs oxygen—thus fulfilling the rôle of a secretion deemed necessary by various physiologists (Paul Bert, Müller, Bohr, Haldane and Lorrain Smith, and others) to account for pulmonary respiration; (3) that it becomes, also in this location, the albuminous (96 per cent.) constituent of hemoglobin and the red corpuscles, the identity and source of which physiologists have failed to identify, and (4) that this albuminous constituent of the hemoglobin which I have termed "adrenoxidase" owing to its source, the adrenals, and to its identity as oxidase, is distributed by the red corpuscles to all parts of the body as an oxidizing substance. C. E. DE M. S.]

This interpretation explains the phenomena that attend the use of adrenal extracts, adrenalin, etc., in therapeutic doses. The rise of temperature noted by Morel, Lépine and the concomitant rise of temperature and increased metabolism noted by Oliver and Schäfer are due to increased oxidation. It accounts also for the rise of blood-pressure, since increased metabolic activity—excited directly by the adrenal principle besides that due to general oxidation—of the muscular coats of vessels is manifested by contraction, and, therefore, by elevation of the blood-pressure. The increased power of the heart is the obvious outcome of increased metabolism in the myocardium, precisely as it is in the vascular muscles, while the slowing of its action is due to the greater diastolic expansion that attends increased functional vigor and the greater resistance the blood-column offers as a result of the increased blood-pressure.

The same process explains the phenomena produced by adrenal extractives which appear quite discordant from its more familiar effects on the blood-pressure, the heart, etc. They produce arteriosclerosis by causing excessive contraction of the vasa vasorum, from which the arterioles receive their blood. The walls of the arteries these minute vessels nourish being partly or completely deprived of blood, they degenerate, and sclerosis follows. Glycosuria is also the result of excessive metabolism; the pancreas, as are all other organs, being rendered overactive, its ferments are secreted in excess. Amylopsin being one of these, the hepatic glycogen is converted into sugar in quantities exceeding the needs of the tissues, and the unused sugar is eliminated by the kidneys. Increased metabolism likewise explains the abnormal activity of the lachrymal and salivary glands.

Finally, the antagonistic effects of these agents are accounted for by the fact that, while the intestinal vessels are contracted through the excessive metabolic activity produced in their muscular coats, the intestines themselves are relaxed because the volume of blood supplied to them is reduced by the undue constriction of their vessels.

[The participation of the adrenal secretion in this phenomenon is shown by the fact that the supposed inhibitory action of the sympathetic on intestinal movements (which, as I have shown in "Internal Secretions," is merely an experimental phenomenon brought about by excessive constriction of the intestinal vessels) is offset by severing the nerves to the adrenals. This fact, first observed by Jacobi (Arch. f. exper. Pathol., Bd. xxix, S. 171, 1892), proves, from my viewpoint, that two sources of vasoconstriction (manifested by elevation of the blood-pressure) must always be taken into account: (1) that due to vasomotor nerves, and (2) that due to increased activity of the adrenals. It is by producing a similar constriction of the arterioles that opium and its analgesic alkaloids cause constipation and relieve pain—according to my views. C. E. DE M. S.]

Physiology of Local Action.—The local application of an adrenal principle, adrenalin, epinephrin, etc., causes such marked contraction of the vessels that their lumina, when applied over small vessels, may become obliterated, thus arresting totally the flow of blood. The tissues become very pale, therefore, and even blanched. These effects, however, are of short duration. Mucous membranes are similarly affected; hence, the frequent use of adrenal extractives on the nasal mucosa and the conjunctiva. The constrictive effect on the blood-vessels is due to a direct action on their muscular elements; applied to the eye, adrenal extractives also produce contraction of its muscles. Hence, the dilatation of the pupil, the wide separation of the eyelids, and apparent protrusion of the eyeball. From my viewpoint, the contraction of the vessels produced by adrenalin and the resultant blanching are due to the increased metabolic activity it awakens temporarily in the vascular and other tissues to which it is applied.

[The process does not differ from that which obtains in the blood. It is that of exaggerated oxidation in which the adrenalin, as I have pointed out, plays the part of a catalyzer. Poehl found that the adrenal active principle was endowed with catalytic properties. This enables it to activate greatly the process of oxidation without being itself rapidly consumed—its action recalling that of a ferment. Jolles showed, moreover, that the catalytic activity of a given volume of blood corresponded with the number of red corpuscles it contained. These corpuscles being the carriers of hemoglobin, which, in turn, contains the adrenal principle, as I have shown, adrenalin, when applied to the tissues, acts as if a large

amount of oxyhemoglobin had been concentrated upon it. C. E. DE M. S.]

PREPARATIONS AND DOSE.—The preparations most generally used are the dried gland, the *glandulæ suprarenalis siccæ* of the 1905 U. S. P., available in tablets or powder, the dose of which is 2 to 10 grains, and the active principle *epinephrin,* now generally accepted as the official name for several proprietary preparations, such as adrenalin, suprarenalin, supracapsulin, adrin, etc. Synthetic epinephrin is also available, but there is no ground upon which it should be given preference over active principle obtained from the adrenals. As shown by Shultz, Cushny, and others, the synthetic products are about one-half the strength of the natural. Though the latter also vary in physiological activity somewhat, the solutions available are uniformly of 1:1000, the doses of which are: *By the mouth,* 10 to 30 minims; *intramuscularly* or *hypodermically,* if the region is massaged, 3 to 15 minims, always in free dilution with saline solution. *Intravenously,* it should only be given drop by drop in large dilution with saline solution, the latter being used as in hypodermoclysis. The use of strong solutions of 1:1000 solution intravenously is always fraught with considerable danger.

The writer urges that adrenal preparations be used greatly diluted, as this reduces materially the toxic action, even of the same dose; he also pleads for caution in the estimations of the individual reaction in the given case, especially the exact state of the heart and the vessels. He warns against intravenous injection, and emphasizes the necessity for extreme care in injecting the preparation where it might get into a vein. The vaginal portion of the uterus can be rendered anemic effectually and safely by injection of only 10 c.c. of 200 c.c. of salt solution containing merely 1 c.c. of the 1 per thousand solution of suprarenin—there is no need to use a stronger concentration. Neu (Zentralbl. f. Gynäk., July 24, 1909).

Two fatal cases due to the use of suprarenin injected into the cervix for operative purposes. The author and other surgeons and dentists have made use of this drug in thousands of cases for local anesthesia, combined with other drugs, and have experienced no bad effects. As to the cause, there is no fixed poisonous amount of this drug; this varies with the individual, and with the way in which it is used. The writer uses a very weak solution injected in considerable amount. It is not the amount of the drug or of the solution used, but the concentration of the solution, that does harm. A large amount of a weak solution can be used without danger, while a small amount of a strong solution will be fatal. The method in which the material is introduced is also of importance. Injected intravenously it will have an immediate bad effect, while applied locally or subcutaneously it will be well borne. The author combines it with a ½ per cent. solution of novocaine, and to 100 c.c. of this solution he adds 0.64 Gm. of borate of suprarenin. The drugs are made up into a tablet and the solution made freshly for each operation. He has no fear of using as much as 125 c.c. of this solution for an operation. Braun (Zeit. f. Gyn., July 24, 1909).

As I pointed out in 1907, it is very doubtful whether epinephrin, adrenalin, or any of the adrenal active principles are physiologically active in so far as the general system is concerned. This I attribute to the fact that gastric secretions give the oxidase reactions (guaiac, etc.), thus showing that they can oxidize them before they reach the circulation at all, and are thus deprived of their physiological properties.

Adrenalin injected subcutaneously or into the peritoneum in laboratory animals has a marked toxic action and no adrenalin appears in the urine. On the other hand, 20 times this dosage and more, given by the mouth, causes no signs of toxic action, while considerable amounts of adrenalin are eliminated in the urine. The author thinks that under the influence of the digestive juice and of the mucosa the adrenalin becomes bound in some way which deprives it of its physiological and toxic properties. Further research seems to demonstrate that the deintoxication of adrenalin occurs not in the liver, but in the gastrointestinal canal. Falta (Wiener klin. Woch., Dec. 23, 1909).

This does not apply to the dried gland, probably because the active principle is bound up in organic combination. S. Solis-Cohen found, moreover, that, by masticating the dried gland without swallowing it, the physiological effects manifested themselves. The active principle proper, adrenalin, etc., are, nevertheless, absorbed from the colon, especially when administered with saline solution.

Each of the epinephrin preparations, suprarenalin, adrenalin, etc., available is also conveniently put up as an *inhalant, ointment,* and *suppositories,* the strength being also 1:1000 in neutral oil, petrolatum, or oil of theobroma in the order of the preparations named, and some mild antiseptic to preserve the latter.

UNTOWARD EFFECTS.—In the frog toxic doses produce a temporary paresis, the muscles acquiring marked rigidity. This is ascribed by some to poisoning of the spinal cord, by others to a direct action on the muscles. In mammals large doses given subcutaneously cause excitement, tremor and vomiting, paralysis beginning at the posterior extremities, polyuria, and dyspnea, death occurring either through respiratory failure or cardiac arrest. In the cat, however, which bears larger doses than other animals, the respiration ceases, as a rule, before the heart's action is arrested. This is due to pulmonary edema, according to some authors, and to paralysis of the respiratory centers, according to others. When the poison is injected into a vein the morbid effects are preceded by a very rapid and marked rise of the blood-pressure.

Man is more susceptible to the action of adrenalin than animals. While a subcutaneous injection of 1 dram (4 c.c.) of a 1:1000 solution will hardly affect a rabbit, one-third of that quantity has produced untoward effects in normal as well as in tuberculous subjects (Souques and Morel), *e.g.,* vertigo, nausea, vomiting, severe pain under the sternum similar to that of angina pectoris, and a feeling of constriction about the chest, a rapid pulse, dyspnea, cold sweats, and coldness of the extremities.

Two fatalities following injection of adrenalin into the vaginal portion of the uterus. The first patient was a woman of 47 with total prolapse of the uterus, the vaginal portion of which was much hypertrophied. Under chloroform the fluid, consisting of 1 c.c. of adrenalin solution in 10 c.c. of 0.8 per cent. salt solution, was injected at 3 points when suddenly retching occurred, respiration and pulse stopped, and it proved impossible to revive the patient. Ten days later the same syndrome with instant death occurred in a similar case, the patient being a robust woman of 33 with a hemorrhagic metritis and fibrous hypertrophy of the neck of the uterus requiring wedge resection. Some of the fluid used was injected into rabbits, but showed no injurious by-effects. The dose was very small in these cases,

not more than 0.0003 Gm. of active adrenalin. N. N. (Zentralbl. f. Gynäk., June 19, 1909).

Intoxication may also follow the use of adrenalin when injected into cavities, such as the vagina, the rectum, the urethra, when the mucous membrane is abraded, lacerated, or denuded, thus rendering its absorption possible.

Case in a negro aged 26, male, very rugged, had a stricture of the urethra. After some difficulty the author succeeded in passing a No. 24 French sound. When the sound was withdrawn considerable blood followed it, which greatly alarmed the patient. Thinking to quiet his fears, half a dram of adrenalin chloride (1:1000) was injected. In about thirty seconds the patient became restless and moved about, staggered, and was laid on the couch. He complained of intense pain about the heart, and his breathing was labored and very rapid. The heart-beat was so fast that it could not be counted. The conjunctiva was blanched. Profuse perspiration broke out all over the body, and the extremities became very cold. The man declared that he was dying, and the writer was inclined to believe him. In about five minutes he began to cough and spat up mouthfuls of bloody froth. The coughing and spitting of blood continued for over an hour. The pulse, which had been very hard, became soft and slow.

Morphine, atropine, and nitroglycerin hypodermically were given during the continuance of the alarming symptoms. The patient gradually became quieter, and the symptoms subsided. He slept fairly well the following night and rose the next day very little the worse for his experience. F. C. Bennett (Jour. Amer. Med. Assoc., Nov. 17, 1906).

Case of a man aged 26 weighing 190 pounds, heart and lungs normal, in whom, to arrest bleeding caused by manipulation of the urethra to render a stricture passable, 10 minims of a 1:1000 solution of suprarenal principle were injected through an Ultzman instillator. The patient immediately complained of pain in the stomach, and a condition of profound shock supervened. He complained of air-hunger, vomited, and lapsed into syncope. As the pulse became slower and finally disappeared, and death seemed imminent, $\frac{1}{30}$ grain of strychnine and $\frac{1}{100}$ grain of nitroglycerin were given hypodermically. In ten minutes the radial pulse began to return, and within an hour the patient left the office unassisted. Next day progressive dilatation of the stricture was practised without the aid of the adrenal preparation. Link (Central States Med. Monitor, Sept., 1907).

The prolonged use of adrenal preparations may induce chronic adrenalism, manifested by marked cardiac disorders, especially of the myocardium; dyspnea after slight exertion, tachycardia, high blood-pressure, polyuria, icteric staining of the conjunctiva, and marked increase in weight.

Case of a man who during one year and nine months applied daily to the conjunctiva, as a treatment for conjunctivitis, a solution of adrenalin chloride. Palpitations, with marked increase of the arterial tension, cardiac dyspnea on exertion, and polyuria, were followed by a yellowish tinge of the conjunctiva such as that observed in jaundice. A curious feature of the case was that the patient gained in weight rapidly. Cessation of the instillations and regulation of the diet caused a gradual retrogression of these symptoms, but there remained some cardiac weakness. K. Feiler (Med. Klinik, May 17, 1908).

Local applications are sometimes followed by untoward effects in the tissues to which epinephrin solutions are applied. Repeated applications, especially with the atomizer, of anything but weak solutions (1:10,000) to the nasal cavities or pharynx may give rise to edema of the nasal mucosa, the uvula, tonsils, or pillars of the fauces. This is ascribed by most writers to "violent

vasomotor constriction of the blood-vessels" and the resulting "venous stagnation." In some instances they cause persistent sneezing and acute coryza accompanied at times by severe pain in the upper portion of the nasal cavities.

> Case of a man aged 39, of good habits and good health, except for his periodic attacks of hay fever, who was advised by a lay friend to use one of the well-known preparations of the suprarenal gland, and supplied himself with the remedy and an atomizer in the summer of 1905. He used it several times a day during his attack.
>
> When the hay fever subsided he noticed that there was a fullness in his nose that did not disappear, but, on the contrary, became more marked. He was treated by his physician for a time without relief, and then sought the aid of a rhinologist. The condition refused to yield to any form of treatment, and, symptoms of Eustachian congestion supervening, it became necessary to remove portions of both middle turbinates. After a long course of treatment he went to his home improved, but bearing traces of the condition with him. Two other very similar cases witnessed. B. H. Potts (Jour. Amer. Med. Assoc., Oct. 13, 1906).

Adrenalin, when applied to the gums on cotton-wool—whether to stop bleeding or, as has been recommended in the preparation of cavities, to control the saliva exuding from the mucous glands at the neck of the teeth—should be used with great caution. The cotton-wool with the adrenalin solution should be thoroughly squeezed to remove excess before applying.

> The writer had occasion to witness recently a distinct case of adrenalin poisoning in which it had been used to stop bleeding. Evidently in this case the adrenalin had been applied freely, and, on pressure being used to the pad of cotton-wool, a few drops of the excess adrenalin had been squeezed out. The symptoms were alarming, being not unlike an epileptic seizure, and the patient remained in a collapsed condition for some hours after. Anonymous (Chemist and Druggist; Prescriber, March, 1911).

Some cases have been reported in which sloughing and gangrene of the mucosa occurred. Elderly subjects are prone to this complication, according to Neugebauer. Postoperative hemorrhages are not infrequently noticed after the use of adrenalin, owing to relaxation of the severed vessels.

> A rather extensive use of suprarenal extract in intranasal operations showed that there is a marked tendency toward secondary hemorrhage, the bleeding coming on in from two to four hours after the operation. Letters to a number of specialists brought out the fact that with one exception they all experienced the same trouble. The mixture of cocaine and suprarenal is followed by relaxation sooner than when the suprarenal is used by itself in the majority of cases. After operating in the nose when suprarenal extract is used it is best in every instance to pack the fossa and so be on guard against the secondary bleeding. A less common sequela to the use of suprarenal is an intense coryza induced by the secondary relaxation. F. E. Hopkins (N. Y. Med. Jour., Aug. 25, 1900).

In the larynx, epinephrin solutions cause an uncomfortable dryness by interfering with the formation of lubricating mucus. This is especially distressing to singers. In the eye their use in scleritis and other disorders may be followed by severe iritis. Instillations of a 1 : 1000 solution in the Eustachian tubes have given rise to violent pain in the middle ear, which was renewed whenever the remedy was thus administered. The use of adrenalin solutions, in the form of a spray at least, is contraindicated in infections, owing to the danger of facilitating the entrance of pathogenic germs into the sinuses.

A fresh case of influenza with severe coryza is a distinct contraindication to its use. The drug by causing contraction of the tissues dilates all the cranial sinuses, and, if the patient unguardedly uses his handkerchief while the mucous membranes are under the influence of the drug, bacteria will be certainly blown into the antrum of Highmore, probably into the ethmoid cells and the middle ear, and possibly into the frontal sinuses as well. Empyema of all the sinuses named has thus been caused. J. J. Kyle (Pediatrics, Feb. 15, 1902).

The rôle I attribute to the adrenal secretion in oxidation, metabolism, and nutrition is as applicable to the untoward phenomena as it was to the therapeutic action of the drug. Following the course of events from start to finish, we have at first the effects of excessive metabolism in all tissues: in the cerebrospinal system, excitement; in the muscles, tremor; in the kidneys, polyuria; in the myocardium, violent contractions (palpitations); in the muscular coats of the vascular system, a marked rise of the blood-pressure. The latter in turn aggravates the process by causing congestion and engorgement of the capillaries (which are not, like the arteries, provided with a muscular coat) of all organs, including the lungs, causing edema of these structures and dyspnea. As the contraction of the arteries proceeds, the aorta has to bear the brunt of the centrifugal pressure, giving rise to marked substernal pain. When it becomes such that the arterioles obstruct the circulation the lethal phenomena are initiated: the pulmonary circulation being impeded, oxygenation fails to occur, asphyxia follows, and, the myocardium receiving too little blood to sustain its contractile power, the heart, already hampered by the pulmonary congestion, ceases to beat.

In *chronic adrenalism* the same interpretation obtains, the cardiac phenomena being ascribable mainly to the extra work imposed upon the heart by the resistance of the general vascular tension. The gain in weight is a normal result of increased metabolic activity, *i.e.,* overnutrition.

[In the first volume of "Internal Secretions" (pp. 192 *et seq.,* 1st ed.) I pointed out in 1903 that the overgrowth in acromegaly and gigantism was due to overactivity of the adrenals. The correctness of this view, based on many experimental and clinical facts, was shown by the observations of L. G. Guthrie (Brit. Med. Jour., Sept. 21, 1907), who referred to a series of cases of overgrowth in children—1 personal and 5 from literature, in all of which "adrenal tumors existed." One of these, for instance, a child of 3 years, was prematurely developed and weighed 44 pounds. Guthrie, as I had four years earlier, ascribed the overgrowth to hypersecretion of the adrenals. C. E. DE M. S.]

After *local applications* the morbid effects are all the result of the action of the adrenal principle upon the vessels.

The dryness produced by solutions sprayed into the larynx is due to deficiency of blood supplied to the acini and the resulting inhibition of their function. If this is kept up by repeated applications, the tissues, no longer nourished, may slough off, as has been noticed in the upper respiratory tract of aged subjects. The edema observed in this location is not active, as it is in the lungs, but passive, *i.e.,* due to exaggerated relaxation of the vessels after the intense constriction to which the drug had subjected them. This applies equally well to postoperative hemorrhage, and to the severe pain (due to passive congestion) in the middle ear after instillations in the Eustachian orifice.

THERAPEUTICS.—Addison's Disease.—Textbooks of practice and therapeutics now teach pretty generally that adrenal preparations are of value in Addison's disease. A personal study of the literature of the subject showed that out of 120 cases treated by adrenal preparations 25 had been sufficiently benefited to be restored to health—as far, at least, as the loss of adrenal tissue incurred through the local morbid process would permit.

The one great factor in the treatment of this affection by means of adrenal extractives is to drop their *empirical* use, and it is only (and this applies to the use of any disease) when the importance of this fact will have been thoroughly grasped that the proportion of recoveries will be materially increased. Empiricism here may entail death.

[E. W. Adams (Practitioner, Oct., 1903) refers to a group of 7 cases found by him in literature "in which alarming or fatal results were presumably or possibly due to the treatment." He mentions, for instance, 2 cases reported by a prominent clinician treated with "suprarenal gland extract." The chart notes of the cases include the laconic words: "Alarming collapse. One of the cases began to improve markedly when the extract was stopped." In the original paper reference is made to another case treated by suprarenal extract in which "similar collapse was noted." The dose was not mentioned. Such cases are apt to be regarded as examples of the sudden death sometimes observed in Addison's disease, to which Addison himself, Dieulafoy, Anderson, Bradbury, and others have called attention; but this explanation does not hold. Guiol (Bull. de la Soc. médico-chir. du Var., Dec., 1906), having observed similar signs of intoxication and collapse, tried the "remedy" in a normal subject and obtained the same morbid phenomena. Here, again, we are dealing with fatalities which occurred when the physiological functions of the organs, and, therefore, their mode of action as a therapeutic agent, were but slightly known. C. E. DE M. S.]

The salient guides in the use of these preparations are the *low temperature,* which denotes deficient oxidation and metabolism, and the *weak pulse,* which points to a low vascular tension and inadequate cardiac dynamism. Improvement of a given case is indicated by a gradual resumption of normal conditions in these two directions, and by the return of bodily vigor, with more or less fading of the pigmentation. As a rule, the more these various morbid phenomena are marked, the larger will be the initial dose required. In other words, marked hypothermia, a very feeble pulse, advanced bronzing, and great debility will indicate that a mere vestige of both adrenals is still active; the dose indicated, then, is that which will supply enough additional principle to *raise the temperature and the blood-pressure to normal,* but *not beyond.* A study of the 120 above-mentioned cases has shown that 3 grains (0.2 Gm.) of the desiccated gland three times daily was the most satisfactory dose to start with. If this fails to raise the temperature and the pulse tension or improve the case, the dose should be increased by 1 grain *per day* until it does, the case being watched closely. As soon as the normal temperature is reached, the dose should no longer be increased, unless a tendency to recurrence of the hypothermia (gradually as the adrenals are being destroyed by the local morbid process) should render it necessary. In less advanced cases the initial doses should be correspondingly small, 2 or even 1 grain of the extract being administered three times daily, the dose decreasing in proportion as the disease is less advanced.

Can we expect a cure from adrenal preparations? In most cases of Addison's disease the local process is tubercular—often limited to the adrenals. A number of examples suggest, however, that the tubercular process itself was benefited, and even cured, by the use of adrenal extract. This is quite in accord with the view I have advanced, and sustained by considerable evidence ("Internal Secretions," vol. i, 1903, and vol. ii, 1907; see also N. Y. Med. Jour., Feb. 20 and 27, 1909) that the adrenal secretion sustains the efficiency of the immunizing mechanism.

A number of cases are on record in which, after apparent recovery, the cases died suddenly soon after ceasing the use of adrenal preparations. It is evident that even the possibility of curing the morbid process in the adrenals does not replace the destroyed adrenal tissue. It is here that grafting would be of curative value, but only provided *small fragments of adrenal tissue* be inserted, and gradually increased in number until the temperature and pulse indicate that compensation for the functionless areas in the adrenals has been increased.

The 120 cases analyzed showed also, and my own experience has further demonstrated, that what is generally known as "adrenal extract," but which, in reality, is the desiccated adrenal gland (the *glandulæ suprarenales siccæ* of the U. S. P), is by far the most satisfactory agent to use. Injections of adrenal fluidextracts are exceedingly painful—a fact which compromises the issue by introducing the element of shock—while the active principles, epinephrin, adrenalin, suprarenalin, etc., sometimes fail altogether to act, owing to their becoming oxidized and rendered inert while being absorbed. The fresh gland is, as a rule, repulsive to the patient, and tends to aggravate the tendency to nausea and vomiting.

See, also, Addison's Disease, Treatment of, this volume.

Shock, Collapse, and Surgical Diseases.—This is another condition in which adrenal preparations show prominently their influence on metabolism. The function I ascribe to the adrenal secretion (to take up the oxygen of the air, and be carried to the tissues where its active principle augments greatly the activity of this gas) involves the conclusion that it is a prominent factor in the sustenance of the body heat, a fact demonstrated by Reichert, Lépine, Morel, and others. Now, Kinnaman, in a comprehensive study of the temperature relationship to shock, concluded that as shock increased in severity the most uniform progressive factor was the fall in temperature. He states that "in one series [of cases] the fall in temperature was the sole cause of shock." The results of Crile with adrenalin in salt solution given very slowly and gradually for a considerable time thus find a normal explanation in my interpretation of the rôle of the adrenal secretion. He supplied the organism precisely with the substance which sustains the vital process in the tissue-cells. Indeed, he resuscitated animals in this manner—with simultaneous artificial respiration—fifteen minutes after all signs of life had ceased, and was able to keep a decapitated dog alive over ten hours by this same procedure. That it was because the adrenal secretion is able to sustain tissue metabolism, *i.e.*, the vital process itself, that such results were obtained seems self-evident.

The value of adrenalin in raising the blood-pressure, by its action upon the

vascular walls in the state of suspended animation, has been thoroughly established. Introducing the adrenalin into the venous circulation, while easy and practical, had the following disadvantage: the adrenalin first came in contact with the vessels having the least power of influencing the blood-pressure, and before a material rise could be effected by its action upon the arteries it was necessary that the solution should pass through the right heart, the lungs, and then back to the left heart on its way to the aorta, then finally affecting the coronary arteries. In a previous research it was found that this too often caused an accumulation of solution and blood in the dilated paralyzed chambers of the heart, defeating resuscitation.

It seemed reasonable to suppose that the most direct and effective way of producing a coronary pressure amounting to 40 or more millimeters of mercury was by introducing a solution of adrenalin into the arterial system toward the heart. In this way the moment the adrenalin was introduced it caused a contraction of the strong arterial walls, and began to produce an arterial pressure which was communicated directly to the coronary arteries without first passing directly through the already distended and paralyzed chambers of the heart and through the lungs. These considerations were strongly impressed upon the author by a clinical case of suspended animation in the course of a cerebellar operation on a child, which was unexpectedly resuscitated by centripetal arterial infusion of adrenalin.

The following will serve as an illustration: An animal was killed by chloroform. A cannula was inserted into the femoral artery and directed toward the heart. After five minutes, artificial respirations were begun, and the saline solution was given into the tube near the cannula. A few seconds later the blood-pressure began to rise steadily; then a few firm pressures upon the thorax over the heart caused a leaping up of high pulse waves, and at the end of three-quarters of a minute the heart beat vigorously, driving the blood up into the infusion bottle, which had been to the height of 5 feet. The saline injection and the cardiac massage were discontinued, and in a few minutes irregular respirations began slowly, and increased in force and frequency until the normal was established. The animal was then definitely killed.

In general, the following sequence of return of the various functions and reflexes was exhibited: vasomotor action, respiration, corneal reflex and knee-jerk (tendon reflexes in general), kinking, cutaneous reflexes, partial or complete contraction of the pupils, and light reflex. Crile (Amer. Jour. Med. Sci., April, 1909).

This applies not only to shock, but also to **surgical heart-failure, collapse** from hemorrhage, **asphyxia**, and **submersion.** The adrenal principle (suprarenalin, adrenalin, etc.) promotes energetically, as a catalyzer and constituent of the hemoglobin, the intake of oxygen and its utilization by the tissue-cells, including the muscular elements of the cardiovascular system, and thus causes them to resume their vital activity. It should be very slowly administered intravenously, 5 minims of the 1000 solution to the pint of warm (105° F.) saline solution. In urgent cases 10 drops of suprarenalin or adrenalin in 1 dram of saline solution can be used instead, and repeated at intervals until the heart responds. Artificial respiration hastens its effects.

Intravenous adrenalin injections are particularly indicated in acute dangerous disorders of the heart and respiration. It constitutes the most active remedy in the severe collapse that sometimes follows spinal anesthesia and narcosis, and is also of service in severe **surgical shock.** In case of **hemorrhage** and in peritonitis a combination with chloride of sodium infusions is recommended. Whenever patients are rendered insensible, adren-

alin should be kept on hand besides other excitants, such as camphor, etc. The dose for intravenous injection is ½ to 1 c.c. of a 1 per cent. solution undiluted, or diluted 20 times—that is to say, from 10 to 20 drops in 11 of physiological salt solution. Kothe (Therap. der Gegenwart, Feb., 1909).

The use of suprarenal preparations in cases of acute cardiovascular **collapse** highly recommended. Their action is prompt, and their use may often tide the patient past the danger point. The writer reports 7 cases in which he has had good results from their use. In 1 of the cases he failed to follow up the remarkable benefit from a single injection, and ascribes the fatal outcome to his failure to continue the injections. Sohn (Münch. med. Woch., Bd. xxiv, S. 1221, 1909).

In **collapse** from weakness of the vasomotor center, such as is liable in **pneumonia, diphtheria,** and **peritonitis,** good results may be obtained with a suprarenal preparation injected into a vein, or, diluted with salt solution, injected subcutaneously. Case of uncomplicated **ileus** in which by this means it proved possible to tide the apparently moribund patient past the danger stage after two days of fecal vomiting, and thus permitted a successful operation. Heidenhain (Deut. Zeit. f. Chir., April, 1910).

Research showing that epinephrin has no cumulative action. Its action only on direct contact. The continual infusion of a weak solution of epinephrin may prove a useful measure in therapeutics. It is thus possible to send the solution continuously into a vein and thus keep up the blood-pressure permanently while this is being done—the effect being dependent on the concentration of the solution, not on the absolute amount of epinephrin infused. Straub (Münch. med. Woch., June 27, 1911).

Reference was made under "Untoward Effects" to the dangers attending the use of the adrenal principles in **surgery** to produce ischemia at the seat of operation. Though such effects are not often met with, the fact remains that they should be borne in mind and the principle that it is the free dilution of supracapsulin, adrenalin, etc., that promotes safety. Surgical operations can also be performed without loss of blood, except from the larger vessels, in almost any organ by injecting locally 8 to 10 minims of a 1:1000 solution in four or five times the same quantity of saline solution. Care should be taken not to inject too large a dose lest the untoward effects described earlier in this article occur. Solutions of 1:10,000 or even 1:100,000 are quite sufficient sometimes to produce a bloodless field by causing local constriction of the blood-vessels.

Toxemias and Bacterial Infections.—This is a recent and important development of organotherapy. Abelous and Langlois, Charrin, Oppenheim, and others have laid stress on the antitoxic functions. The process through which this protective rôle was carried out by these organs being admittedly unknown, I submitted in 1903 and 1907 ("Internal Secretions") evidence tending to show that the adrenals and thyroid were the sources of two substances as prominent agents in the immunizing process—the thyroid carrying out, we have seen, the rôle of opsonin (confirmed by Fassin, Stèpanoff, and Marbé), while the adrenal secretion acted as amboceptor. While I do not regard these two agents as the sole participants in the immunizing process, the fact remains that the addition of either of them to the blood enhances to a certain extent its functional activity. Especially is this the case in view of the fact that adrenal secretion, as previously stated, serves to sustain oxida-

tion and tissue metabolism. By doing so it activates the functions of all tissues, including those concerned with the production of protective substances. The blood thus finds itself richer in these substances and more active as a germicidal and antitoxic agent.

In **diphtheria** the writer has seen undoubted improvement in the general condition from 2 to 3 c.c. of the commercial suprarenin solution being injected three to four times a day. The action is not so transient as after intravenous use. The maximum rise in blood-pressure can be observed after one to two hours, and the effect may last as long as seven hours. The frequency of hemorrhage from the nose or throat is not diminished, nor is the pulse rate altered. The injections are frequently painful; hence, a moist dressing should be applied. A local anemia may appear at the site of injection, which may persist for hours. Abscesses, infiltrations, or gangrene did not occur, nor could any deleterious influence upon the kidneys be observed. In some cases a temporary glycosuria was noticed, which may lead to the excretion of as much as 2.6 per cent. sugar. In fatal cases the arteries were studied most carefully, but no lesions could be detected. Eckert (Therap. Monats., Aug., 1909).

While the normal average of epinephrin content in the human suprarenals is about 4 mg. (in arteriosclerosis it is 5.8 mg. and in chronic nephritis 5.79 mg.), in septic disturbances with low blood-pressure the average found was only 1.5 mg. This loss of epinephrin was manifest in pneumonia, puerperal fever, meningitis, and other septic processes, showing that it is merely a general reaction of the suprarenals to infections. The changes in the suprarenals may be a swelling of the parenchyma, cystic degeneration, or development of hemorrhagic infarcts—all the changes being serious and explaining the disturbance or total arrest of suprarenal functioning in infectious diseases. This leads to an abnormally small portion of epinephrin in the blood, and this is clinically manifested by a lessened blood-pressure. The collapse in septic affections is probably due chiefly to the lessened blood-pressure resulting from the acute suprarenal insufficiency. Goldsieher (Wiener klin. Woch., June 2, 1910).

Infectious diseases constitute the principal field in which the adrenalin treatment is of service, and the writer has employed adrenalin successfully in many cases of severe collapse in connection with **scarlet fever, pneumonia,** and **typhoid fever.** He does not hesitate to use large doses. He invariably administers it by subcutaneous injection and has observed no after-effects. Kirchheim (Münch. med. Woch., Dec. 20, 1910).

Adrenalin, injected intravenously, in saline solution, is indicated in the treatment of **peritonitis,** used continuously. The action of adrenalin on the diseased organism must be borne in mind. By using the drug in very dilute solution weakened systole becomes strengthened and in time becomes normal in force. The weakened heart and lowered blood-pressure of peritonitis, also due to a toxic substance, indicate the same measure. Holzbach (Münch. med. Woch., May 23, 1911).

One of the active principles, supracapsulin, adrenalin, etc., may be used advantageously in **infectious diseases,** but to avoid untoward effects it is best given well diluted—10 to 15 drops of the 1:1000 solution in not less than 1 dram of water, administered very slowly. If given intravenously it is preferable to administer the saline solution as usual, and then to introduce the needle of the hypodermic syringe into the rubber pipe, injecting a drop of the adrenal active principle (preferably supracapsulin 1:1000) into the stream of saline solution at short intervals. In this manner much more adrenal principle can be introduced with a minimum of danger.

The recognition of the antitoxic property of the adrenal active principle has recently caused it to be employed as an antidote in **strychnine poisoning,** a fact pointed out by Abelous and Langlois in 1898. These authors also found it to oppose the toxicity of **nicotine,** while Oppenheim obtained similar results with **phosphorus.**

Exner has shown that intraperitoneal injections of adrenalin diminish the rate of absorption of **strychnine** introduced into the stomach, and the writer, therefore, decided to try whether adrenalin given by the mouth would exert a similar effect. He first found that adrenalin could exert its vasoconstrictor action after the arteriolar wall has been subjected to the action of **cyanide of potassium,** and then studied its effects upon rabbits poisoned by the cyanide. He was able to bring about recovery after longer periods than in rabbits which had not received adrenalin. He recommended the following procedure for cases of **cyanide poisoning** in man. Adrenalin should be given immediately, 9 c.c. (*i.e.,* 3 drams) of the 1:1000 solution diluted to 90 c.c. saline solution; then Martin and O'Brien's antidote if available. This consists of 30 c.c. (1 ounce) of a 23 per cent. solution of ferrous sulphate, 30 c.c. of 5 per cent. solution of caustic potash, and 2 Gm. (30 grains) of magnesia. The first two solutions should be kept in hermetically sealed phials. The three substances should be mixed when required and immediately taken. The principle of the method is the formation of Prussian blue, which is practically innocuous. The stomach should then be washed out and a further dose of about 5 c.c. (1½ drams) of 1:1000 adrenalin solution diluted to 50 c.c. should be given. A brisk saline purge is also recommended, to be administered soon afterward. J. L. Jona (Intercol. Med. Jour of Austral., July 20, 1909).

Adrenalin found experimentally to counteract the toxic symptoms induced by **strychnine** in the frog. Similarly, if adrenalin and strychnine are injected, guinea-pigs will tolerate several times the fatal dose of the latter drug. The action of adrenalin is actually antagonistic and not dependent on vascular contraction, with slower absorption, as some authors claim, since other poisons are not affected in their toxicity. The antagonism is very similar to that between atropine and muscarine. Falta and Svcovic (Berl. klin. Woch., Oct. 25, 1909; Merck's Archives, Jan., 1910).

Postoperative Intestinal Atony.—To the adrenals seem also to belong the credit of offering the opportunity to antagonize this disorder. When in 1903 I submitted the opinion that the thyroid secretion enhanced the activity of the adrenals—a view since sustained by several experimenters—and that the adrenal secretion, on the other hand, influenced the functional activity of the pancreas, pituitary body, and other organs, the statement created some surprise. This feeling died out, however, when, three years later, Starling termed *hormones* a group of substances secreted by various organs which could enhance the functions of other organs. Precisely as I had previously held, these hormones were secreted, according to Starling, by the organs which produced them in the course of their normal functions, and reached the distant structures they influenced through the intermediary of the blood. What I termed the *adrenal system* owed in great part its functional activity to this chemical co-ordination: the adrenal secretion being especially prominent in the process owing to the function I attributed to it, viz., to sustain oxidation and metabolism as a constituent of the hemoglobin molecule.

Bayliss and Starling termed *secretin* a hormone formed in the intestinal mucous membrane under the influence of the hydrochloric acid from the stomach, which is the chemical excitant of the pancreatic secretion. Now, from my viewpoint, this is not a specific excitant; I showed in 1907 (vol. ii, "Internal Secretions," p. 861) that it presented several of the properties of adrenal extractives. We are dealing, therefore, not with a local product, but with a component of all tissues (being as such what Starling has termed a "mamma hormone"), and which when present in unusual quantities in any organ is capable of enhancing correspondingly its functional activity owing to its influence on local oxidation and metabolism.

Another hormone has been obtained from the gastric mucosa by Dohon, Marxer, and Zuelzer (Berl. klin. Woch., Nu. 46, 1908), which was found to enhance intestinal peristalsis. But inasmuch as it is (from my viewpoint) a ubiquitous component of all tissues, and the difficulty of collecting it during digestion being obvious, search for it elsewhere suggested itself. It was found in ample quantities in the spleen—that junk-shop in which red corpuscles (which, as I suggested in 1903, are the common carriers of the adrenal principle) are broken up along with other cells. That the splenic hormone referred to is not purely the adrenalin-laden albuminous constituent of the hemoglobin derived from red corpuscles is self-evident, since leucocytes with their nucleoproteid granulations, their trypsin-like cytase, and other ferments are also broken up in the spleen. The fact remains, however, that this splenic hormone specifically stimulates intestinal peristalsis to a degree so remarkable experimentally that it may be readily seen in the exposed intestine of experimental animals ten to fifteen minutes after an intravenous injection.

The applications of this peristaltic hormone in surgery are mainly in those conditions of intestinal paresis following operations on the intestine, and particularly where purgatives, castor oil included, bring on no results. It is also indicated in all forms of stubborn constipation due to intestinal atony.

Miscellaneous Disorders.—The foregoing disorders may be said to represent those in which adrenal preparations are more effective than any other preparation at our disposal. There are several others, however, in which they will probably prove of considerable value, when sufficient trial of them in practice will have warranted a final pronouncement. These are:—

Hemorrhage from the pharyngeal, esophageal, gastric, or intestinal mucous membrane. Here the mastication of adrenal substance or the use of powdered adrenal substance in 5-grain capsules arrests the flow, by causing active metabolism in the muscular elements of the arterioles of the mucosa and constriction of these vessels. The active principle, epinephrin, supracapsulin, etc., has also been given by the mouth in 10- to 15- drop doses.

To avoid **hemorrhage** during the removal of placental rests after abortion the writer exposes the cervix and practises deep injection of the following solution into several points of the cervical tissue,—either 1 c.c. of 1 per cent. or 2 c.c. of ½ per cent. cocaine solution to which 3 drops of 1:1000 adrenalin solution has been added. After waiting ten minutes, the operation of

emptying the uterus is practically bloodless and the organ is firmly contracted, though patency of the cervix remains. O. Grasser (Zentralbl. f. Gynäk., June 19, 1909).

The writer has seen within the past year 5 cases of vicarious **hemorrhage,** 1 of the rectum, from the inner canthus of the nose, etc., in which he prescribed the suprarenal extract—adrenalin 1:1000, giving 15 drops every three hours until it ceased—and secured prompt relief. J. W. Irwin (Med. Brief, Aug., 1911).

Sthenic cardiac disorders with **dilatation** of the right ventricle, dyspnea, and possibly cyanosis and edema, owing to the direct action of the adrenal principle on the right ventricle and improved oxidation and metabolism in the cardiovascular muscles and the tissues at large. Tablets of from ½ to 1 grain of the desiccated gland can be taken after meals.

Asthma.—To arrest the paroxysms, by augmenting the pulmonary and tissue intake of oxygen and the cardiovascular propulsion of arterial blood. From 5 to 10 minims of the 1:1000 solution of suprarenalin or adrenalin in 1 dram of saline solution should be injected hypodermically, massaging the part so as to insure absorption of the solution.

Five cases in which remarkable benefit was obtained from adrenalin in acute attacks of **asthma.** No evil effects were observed, even when the adrenalin was injected a number of times. The action is analogous to that of atropine on the vagus, although the adrenalin acts on the sympathetic. Jagic (Berl. klin. Woch., March 29, 1909).

Effusions.—To prevent the recurrence of serous effusions in the pleura, the peritoneum, the tunica vaginalis, etc., after aspiration, by reducing the permeability of the local capillaries and restoring the circulatory equilibrium. From 8 minims to 2 drams (according to the size of the cavity) of suprarenalin or adrenalin, in four times the quantity of saline solution, should be injected into the cavity.

Disorders of Pregnancy and Parturition.—The most useful employment of adrenal preparations in disorders of this class is in **obstinate vomiting of pregnancy.** This was suggested by the frequency and obstinacy of vomiting in Addison's disease and the beneficial influence of adrenal gland over this symptom. The benefit is probably due to the more active destruction of toxic wastes—which are increased during pregnancy owing to the presence of the fetus—a function in which we have seen the adrenals take part.

Very severe case in which all other methods of treatment, hygienic, psychic, and medicinal, had been tried without avail. Believing that the insufficiency of the suprarenal capsules might play an important part in this condition of **autointoxication in pregnancy,** the writer administered to the patient a preparation which comprised all the substances contained in the suprarenal capsules, using tabloids of suprarenal capsule. An immediate amelioration of symptoms was noticed, and in two days' time the vomiting had stopped entirely. The patient continued well at the time of writing, taking 1 tabloid each day. T. Silvestri (La Riforma Medica; Med. Record, Sept. 11, 1909).

Severe case of **hyperemesis gravidarum** of more than two months' duration treated with marked success by means of adrenalin in small doses. Various remedies had been tried, and artificially induced labor was seriously contemplated. In whatever way the drug acts—whether by neutralizing the toxins produced in pregnancy, by toning up the nervous and muscular system, as a stimulant of tissue change, or as a

regulator of the vasomotor system, or in any of the other methods which have been theoretically suggested—the author is convinced of the great therapeutic value of adrenal principle in the obstinate vomiting of this class of cases. S. Rebaudi (Gazz. degli Osped.; Zentralbl. f. Gynäk., Nu. 44, 1909).

Cancer.—The fact that the cancerous growths in mice and rats had been caused to disappear by the injection of the active principle into these growths suggested that the latter might also prove efficacious in man. About all that can be said for the present is that the results warrant further trial.

The writer reports experiments on animals carried out in the laboratory for cancer research under Professor Lewin. The injections were made into the growth. Having observed accidentally that under injections of very small quantities of adrenalin undoubted carcinomatous as well as sarcomatous tumors in mice and rats (which came from Ehrlich's Institute) had completely disappeared, he inoculated large series of animals with cancerous and sarcomatous material and treated immediately afterward with adrenalin, while the control animals were not treated. After a few weeks the tumors of the animals not treated increased rapidly, while the tumors of the animals treated with adrenalin grew scarcely to the size of a pea and finally disappeared altogether. In 100 of these animals a recurrence was observed only twice in the course of a few months.

Of course, there are undeniable differences between the **malignant tumors** of mice and men, but there was, at least, a possibility that human tumors could be influenced in a similar way. Reicher (Deut. med. Woch., Nu. 22, 1910).

Second series of experiments in the König Charité on private patients on a larger scale, based on the foregoing experiments in animals. The writer gave to men an average of 0.2 to 0.3 Gm. to begin with and increased up to 1 Gm. of the original solutions of adrenalin, selecting cases which did not suffer from bad heart disease or calcification of arteries. The best results were obtained in a boy of 12 years who suffered from **sarcoma** of the vertex. Within three and a half weeks the tumor was reduced to one-third of its size. The remaining third was made to disappear under the Christian Müller method of X-rays and high frequency combined. Since six months the tumor has undergone complete retrogression; no recurrence has occurred.

The writer also treated several cases of **malignant lymphoma.** These were mostly patients suffering from mediastinal tumors and internal metastatic growths, so that he could only see whether the visible tumors were decreasing under treatment. As a rule, he succeeded in reducing them to about half or one-third of their size during the time the patients were in the hospital. But, of course, life was not prolonged in these cases.

He has since tried to treat other inoperable tumors, among others a **melanosarcoma,** which was identified as such under the microscope. It was a metastasis in the groin which occurred one and a half years after excision of the primary tumor on the dorsum of the foot. Within one and a half months it had increased to the size of of a man's fist. In three months he was able to reduce its size very little, but, at least, it has become stationary, while before it was growing very rapidly. It is remarkable that during the treatments the patients increased much in weight—up to 14 pounds in his series. There must be a constant anomaly of metabolism somewhere. Reicher (Berl. klin. Woch., Nu. 20, 1911).

[The last remark is suggestive in view of the explanation of the function of the adrenal secretion I have submitted, viz., that it governs metabolism and nutrition, as shown in these cases by the marked increase in weight. C. E. DE M. S.]

The desensitizing of the skin by means of adrenalin permits the use of

nearly double the dose of the **X-rays** for a period of from fourteen to eighteen days. The most important indication for this method is the treatment of **malignant tumors** situated subcutaneously. Reicher and Lenz (Münch. med. Woch., June 13, 1911).

Osteomalacia.—In osteomalacia the adrenal preparations find a normal indication in view of their stimulating influence on metabolism and, therefore, general nutrition, in which the osseous system must normally partake. This beneficial process is further enhanced by the fact that the thyroid apparatus is itself stimulated through the same cause, and that the thyroid secretion, as shown by Macallum, Parhon, and others, actively promotes calcium metabolism.

Case of non-puerperal **osteomalacia** treated with adrenalin. Slight improvement was evident about the sixth injection, but it proved transient, and recurrence of severe symptoms compelled castration, which proved promptly successful. One ovary was found in cystic degeneration; the other was enlarged and adherent. The details of 22 other reported cases of osteomalacia treated with adrenalin have shown that in each of the 14 cases in which improvement was observed a turn for the better was evident after the first or second injection. S. Stocker, Jr. (Correspondenz-Blatt f. Schweizer Aerzte, July 1, 1909).

Six cases of **osteomalacia** treated by the injection of adrenalin, employing a solution of 1:1000. Injections were made daily in the subcutaneous tissue of the abdominal wall under strict antiseptic precautions. The temperature and pulse of the patient and her blood tension were observed and recorded daily. The doses varied from 0.5 to 1 c.c. Although the injections were somewhat painful, no local reaction followed. Some of the patients showed decided reaction in the redness and injection of the face, with altered conditions in the pupil. Most of the patients received 40 or more injections. Considerable improvement followed this treatment. Englander (Zentralbl. f. Gynäk., Nu. 13, 1909).

Since Bossi (1907) used adrenalin in the treatment of **osteomalacia,** some 20 cases have been reported. The writer calls attention to the case of a woman 38 years old in which the adrenalin showed excellent results not only in relieving the symptoms, but healing the bone and straightening of the deformity, while causing disappearance of pain and return of function. The treatment consisted of injections of 1 c.c. of a 100 per cent. solution of adrenalin hydrochloride given every second day for three months. After a short rest the injections were given every third day. When the pains returned the injections were repeated every second day. The favorable results were manifested only after the thirtieth injection. Léon Bernard (Presse méd., Nov. 20, 1909).

Bossi's experiments, *i.e.,* removal of the adrenals in pregnant animals, were repeated by the writer to determine whether any tendency to **osteomalacia** could be detected afterward. He experimented on rabbits and guinea-pigs and was unable to discover evidences suggesting any such influence on the skeleton from unilateral capsulectomy. The animals all aborted, however, in from nine to thirty days; in 2 the abortion was internal, and the embryos were absorbed. This could not have been the result of the operative trauma, as the animals had all recovered completely from this before the abortion occurred. No appreciable morbid changes were found in the ovaries of the animals. Silvestri (Riforma Medica, Aug. 23, 1909).

Case of **osteomalacia** in which symptoms of **tetany** were induced by the injection of adrenalin. The writer suggests that it would be well to make thorough examination of the thyroid gland, the hypophysis, and the suprarenal capsules in every case of osteo-

malacia that comes to autopsy. Marek (Wiener klin. Woch., May 4, 1911).

LOCAL USE.—To check **hemorrhage** from wounds, suprarenalin or adrenalin can be used in various organs.

Bates, Dor, and many other ophthalmologists have introduced the local application of a weak solution to the **conjunctiva** to produce a bloodless field, and also to enhance the local effects of cocaine, atropine, eserine, and other agents used in the eye.

Instillations of 4 to 5 drops of the 1:1000 solution of adrenalin or subconjunctival injections of a smaller quantity causes a primary reduction, followed by a marked increase in tension. Subsequently there is a secondary reduction of tension. These changes are observed in normal as well as glaucomatous eyes. The reaction in normal eyes is not very great, but in glaucomatous eyes it is quite marked. In normal eyes, the effect of the adrenalin passes away in a few hours, whereas in glaucomatous eyes the effect continues for several days.

In a certain number of cases of **glaucoma** the adrenalin produced a lowering of tension, whereas in others it caused attacks of acute exacerbation. Repeated instillations in normal eyes are apparently without much effect, but in glaucomatous eyes there is a marked increase in tension after the final instillation. The result of the combined use of eserine and adrenalin on tension indicate the two opposing forces are at work. Therefore, in eyes that have a predisposition to glaucoma it is advisable to combine eserine with the adrenalin. J. Rubert (Zeit. f. Augenheilk., Bd. xxi, S. 97, 224, 1909).

In 50 cases of **conjunctival hyperemia** from causes varying in nature from simple congestion due to eyestrain to the most severe types of **conjunctivitis,** a single drop of adrenalin chloride solution, 1:5000, in the conjunctival sac almost immediately caused a blanching of the membrane, commencing in about ten seconds, and reaching a maximum in from five to ten minutes, the effect lasting from one-half to two hours, according to the nature of the case. The blanching effect may be obtained by even a solution of from 1:12,000 to 1:10,000 in from thirty seconds to two minutes. A solution of 1:2000 was found to give the best results in operative work upon the eye, causing no irritation that could be noted upon close observation. A 2 per cent. solution of cocaine hydrochloride was used ten minutes prior to the instillation of the adrenalin, when operation was contemplated, in order that the effect of the anesthetic might not be interfered with, thus insuring a painless and almost bloodless result. MacFarlane (Can. Practitioner, June, 1909).

This applies as well to the local use of adrenal extractives in the **nose, pharynx,** and **larynx,** a weak solution of cocaine, 4 per cent., for example, acquiring the power of 15 to 20 per cent. solution, both as anesthetic and styptic. Combined with B-eucaine (5 c.c. of 1 per cent. solution), suprarenalin, or adrenalin, 3 drops of the 1:1000 suffice when injected in small quantities into the tissues, or, applied locally to mucous membranes, are quite effective for **operations** in almost any region, including the urethra. The cocaine and adrenalin solution referred to above is equally effective, the operation being performed after three or four minutes. These solutions are extensively used, especially for dental, uterine, rectal, and urethral operations.

Hemorrhoids.—Bouchard introduced the use of tampons soaked in adrenal preparations for the treatment of this condition. In external piles, especially if there is great distention and hemorrhage, 20 drops of suprarenalin in

2 drams of saline solution applied with a compress relieve greatly the congestion and the pain. A small quantity of cocaine enhances these beneficial effects.

Adrenalin applied to the skin is rapidly absorbed and acts on the vessels in the region. Durable vasoconstriction is obtained by a moderate, graduated application of the adrenalin, renewed according to the effects produced. Too large a dose, at first, paralyzes the reaction. **Hemorrhoids** are benefited when moderate and recent, unless they are the result of portal hypertension. The measure may also fail on account of sclerosis and paresis of the walls of the vessels. The effects of the adrenalin are similar to those of constriction hyperemia. When applied locally it reinforces the local defenses without waiting for general reactions, the outcome of which it is impossible to foresee. The adrenalin is able to act in the depths of the tissues and to aid their defensive efforts, or the adrenalin may arouse them to more effective resistance. Sardon (Annales gén. de méd., Paris, Feb., 1909).

Neuralgia, Sciatica, and Neuritis.—To subdue and sometimes arrest pain in these disorders, by causing ischemia of the hyperemic and, therefore, oversensitive nerves. One to 2 minims of a 1:1000 suprarenalin or adrenalin ointment applied by inunction over the painful area.

Cutaneous Disorders.—Local applications of the 1:1000 solutions of supracapsulin, adrenalin, etc., may be used advantageously to assuage pain and counteract inflammation, which they do by causing constriction of the arterioles. Among the conditions in which they have proven useful are **toxic erythema, urticaria, acne, sunburn, bee-sting, eczema, chilblains, arthralgia, arthritis, varicose veins, burns,** and **X-ray dermatitis.**

Personal case in which adrenalin solution was used with great benefit. In one of these, a woman spilled the contents of a kettle of hot grease over her forearm, causing what looked to be a serious **burn.** This was dressed with a mixture of olive oil, 2 ounces; bismuth subnitrate, 2 drams, and a few drops of carbolic acid and adrenal solution. Within twelve hours there was very little redness, and the following night the patient was able to attend a dance in a short-sleeved dress. Another case was that of a man operating a gasolene engine. Owing to the fact that his engine was not acting properly, he removed the spark-plug and attempted to blow the soot away from the borders of the plug aperture, when the engine back-fired and burned his face to quite a considerable extent. An application similar to the above relieved the acute symptoms within a few hours, and the man was able to resume his work the following morning. The adrenal solution almost immediately relieves the congestion and overcomes the tendency to secondary inflammation. G. L. Servoss (Amer. Jour. Clin. Med., May, 1909).

PITUITARY ORGANOTHERAPY.

"We may assume," wrote Schäfer in 1898, in a review of the investigations on the physiological rôle of this organ, "that the pituitary body furnishes to the blood an internal secretion, and that this internal secretion tends to increase the contraction of the heart and arteries, and perhaps influences nutrition of some of the tissues, especially bone and the tissues of the nervous system." Howell showed, however, that of the two lobes of the organ extract of the anterior lobe produced no effect—a fact confirmed by several investigators—and that the main action of extracts of the posterior lobe was to slow the heart and raise the blood-pressure. Schäfer and Vincent then

concluded, after experiments, that the pituitary contained both a pressor and a depressor substance.

> Doses of 15 to 20 minims of pituitrin produce a perceptible increase in the blood-pressure in from four to twenty minutes, and maintain it from twenty minutes to an hour or even longer, differing in this respect from adrenalin, in which the effect is far more transient. There is a coincident change in the pulse rate, diminishing as the blood-pressure increases and increasing as it falls. However, this change is more gradual, both in its downward course and its return to normal.
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> The rise in blood-pressure varies from 8 to 38 mm., while the pulse rate falls from 4 to 17 beats per minute. No untoward effects were noted in any of the cases in which larger or repeated doses were administered. The inhibitory influence upon the pulse is more lasting than the influence upon the blood-pressure. H. G. Beck and J. J. O'Malley (Amer. Med., Oct., 1909).
>
> The anterior lobe also contains a pressor substance, but its action is usually masked by excessive amount of depressor substance present. By first removing the depressor substance by extracting with alcohol, it was possible to demonstrate a pressor substance in the anterior lobe, chiefly in that portion adjacent to the cleft and which histologically is pars intermedia. Both portions of the posterior lobe contain a pressor substance. Cysts of the pars intermedia and colloid from the cleft, the secretion from the pars intermedia, have a distinct pressor effect. It is scarcely probable that the tissues so entirely different as the pars intermedia and pars nervosa should contain a pressor substance. J. L. Miller, D. D. Lewis, S. A. Matthews (Boston Med. and Surg. Jour., July 6, 1911).

The pressor substance was looked upon as resembling that of adrenal extracts, its application to mucous membranes producing blanching, as is the case with adrenalin. With Herring, Schäfer then found that pituitary extract was endowed with powerful diuretic properties, and that it produced dilatation of the organ. Finally, Herring advanced the theory that the secretion was formed in the anterior lobe and completed in the posterior lobe, and that it then passed into the third ventricle, to mix therein with the cerebrospinal fluid.

> Two conditions, one due to a pathologically increased activity of the pars anterior of the hypophysis (hyperpituitarism), the other to a diminished activity of the same epithelial structure (hypopituitarism), seem capable of clinical distinction. The former expresses itself chiefly as a process of overgrowth—gigantism when originating in youth, acromegaly when originating in adult life. The latter expresses itself chiefly as an excessive, often a rapid deposition of fat with persistence of infantile sexual characteristics when the process dates from youth, and a tendency toward a loss of the acquired signs of adolescence when it first appears in adult life. Experimental observations show not only that the anterior lobe of the hypophysis is a structure of such importance that a condition of apituitarism is incompatible with the long maintenance of life, but also that its partial removal leads to symptoms comparable to those which are regarded as characteristic of lessened secretion (hypopituitarism) in man. Cushing (Jour. Amer. Med. Assoc., July 24, 1909).

From my viewpoint, the prevailing idea that either lobe of the pituitary is a secreting organ was based on an assumption at the start, and has been perpetuated as such. The effects of its extracts are those of the adrenal principle which the posterior pituitary contains; not only does the pressor substance give the actions of chromaffin substance, due to the presence of the adrenal principle, but it produces the

same effects. The functions I have attributed to the pituitary are totally different; but as they do not bear in any way upon the valuable therapeutic effects of this organ, they need not be described in the present connection. As I view it, therefore, pituitary preparations merely afford an additional and efficacious way of administering adrenal preparations. Being bound up in organic combination, the adrenal principle acts with less violence, owing, probably, to the fact that even in the tissues the product injected is decomposed very slowly.

> Herring's view that the colloid fluid passes upward is quite warranted; but this does not prove in the least that it is a true secretion. In fact, Dr. Cushing's own text suggests the contrary. Since the blood-pressure-raising substance is "confined, as Howell has proved, to the posterior lobe," why is it that, as Dr. Cushing says, "after this portion of the gland has been removed, there is no apparent disturbance with the physiologic balance of the body?" Everyone knows that removal of the adrenals or of the thyroid, which produce true secretions, causes marked and even fatal disturbances. Again, the anterior pituitary is regarded by Dr. Cushing as the original source of this secretion; why is it that its extracts are inert? Can we consistently, with him, ascribe acromegaly, overgrowth, etc., to "hypersecretion," and dystrophia adiposogenitalis, Dercum's adiposis dolorosa, etc., to "hyposecretion" of this inert substance? These are but few of the many features which the secretion theory does not meet. C. E. de M. Sajous (Jour. Amer. Med. Assoc., Aug. 21, 1909).

Whichever opinion ultimately prevails concerning its physiological action, the fact remains that pituitary is a valuable remedial agent in many disorders. Its marked advantage is that it sustains the rise of blood-pressure, to which it gives rise much longer than does adrenalin, thus being more reliable in shock and other emergency cases. It seems also to sustain the temperature and the muscular tone, cardiac, vascular, intestinal, and uterine, longer than the adrenal active principle. It possesses also a great practical advantage over adrenalin and other adrenal principles in that it can be administered by the mouth without compromising its effects.

PREPARATIONS AND DOSE.—Pituitary gland is available in drug stores in the form of powder or tablets of desiccated gland. The same preparations of the infundibular, or posterior, lobe, which is the active one therapeutically, can also be obtained. The dose is from 1 to 5 grains three times daily.

A product called "pituitrin" by its manufacturers, in the form of a powder, is available on our market for oral use, the dose of which is given as 10 to 30 grains (0.66 to 2 Gm.).

There is also a liquid extract of the posterior lobe, wrongly termed "infundibular extract," the infundibulum being the pedicle which unites both lobes of the pituitary to the base of the brain. This infundibular extract affects mucous membranes precisely as do adrenal extractives, and should be applied only when diluted in eight or ten times the same quantity of saline solution. It may be given orally in 10- to 30- minim (0.62 to 2 c.c.) doses, or intramuscularly in 3- to 15- minim (0.2 to 0.92 c.c.) doses.

"Vaporole," a liquid extract of foreign origin, issued in hermetically sealed containers, is suitable for intramuscular injections; these are best given in the gluteal region, after the skin has been carefully asepticized.

THERAPEUTICS.—Acromegaly.—The possible value of pituitary extracts in this disease of the pituitary has naturally suggested itself, but, although a few of the symptoms, the headache, lethargy, and amnesia, were relieved in some, no cures were obtained. Analysis of the cases reported as benefited suggests an explanation of its mode of action, however, one quite apart from any functional relationship with the organ as the source of an internal secretion, but entirely in keeping with the presence in the pituitary preparation of adrenal secretion in organic combination. Marinesco observed that it was the extremely violent headaches that were relieved, there being no benefit otherwise, excepting perhaps increased diuresis. Kuh, obtaining no favorable result, withdrew the remedy, but the patient begged to be given the powders again, having found his headache much more intense when he failed to take them. The same observation had been recorded by Cyon, the patient, an obese child of 12 years, having besides lost twenty pounds in weight. What benefit was obtained in 1 case out of 7 cases treated by Kinnicutt was also limited to the headache and neuralgia. Leszynsky, after a prolonged trial in 2 cases, wrote: "While some published reports as to the efficacy of the preparations of the sheep's gland have seemed quite encouraging in so far as the relief of headache and of paresthesia of the hands is concerned, it is the general consensus of opinion that it in no way influences the progress of this disease."

Still, the relief of the headache and paresthesiæ indicates some potent action. This is accounted for if the adrenal principle is considered as the active agent of the pituitary preparations, since, as Langley has shown, it is principally upon the *arterioles* that the adrenal principle acts, a view which has now become classic. Such being the case, the tumor of the pituitary, or the compressed tissues around it, receive less blood through their constricted arterioles, and the sensory terminals of the peripheral likewise. The resulting ischemia of these tissues thus accounts for the diminution of pain—as long only as the remedy is administered.

Cardiac Disorders.—As shown by Rénon and Delille, pituitary gland raises the depressed arterial tension and corrects purely functional disorders of rhythm.

It is recommended in doses ranging from 3 to 6 grains (0.2 to 0.4 Gm.) of the whole gland in myocardial weakness, particularly in that due to infections when the blood-pressure is receding, the pulse is becoming more rapid, and the urine scanty. While less active than digitalis as a diuretic, it, nevertheless, serves a valuable purpose in this connection. It is advantageous in **mitral disorders** when there is hyposystole and in **chronic myocarditis**, particularly that due to alcoholism. It is also useful in the **tachycardia** of certain neuroses and during menopause. These results have been confirmed by Trerotoli, Parisot, and others.

It is contraindicated in aortic affections in any disorder in which high vascular tension prevails, and where there is a tendency to anginal pains, which it tends greatly to aggravate.

Pituitary gland is preferred to adrenal preparations and particularly adrenalin when the action is to be sustained, the former being useful in urgent cases. Rénon and Delille, however, prefer

digitalis, and recommend pituitary gland only when the latter fails. Leonard Williams, on the other hand, deems it superior to digitalis, strophanthus, strychnine, and other classic tonics in what he terms the "**runaway heart of toxic states,**" **influenza, pneumonia, bronchitis,** etc., with tachycardia, but **low blood-pressure,** and in all cases in which there is **posttoxic cardiac debility.** In these cases—which, from my viewpoint, are instances of pure hypoadrenia—Williams regards pituitary preparations superior to any remedy at our command.

In **heart-failure** and **shock,** it has been highly recommended, 15 minims (0.92 c.c.) of the extract being injected intramuscularly. While its virtues would seem to recommend it for the perpetuation of the effects of adrenalin, which are, at best, but temporary, the number of cases in which it has been tried has been too limited so far to warrant an opinion as to its actual value.

Experimental study of the therapeutic value of infundibular extract in **shock, uterine atony,** and **intestinal paresis,** conducted by injecting an extract of it into animals and by observing the effect of the removal of it in part or wholly. It raises the blood-pressure, and even better when the animal is in a condition of shock than in a normal state. Moreover, it keeps the pressure raised for several hours, whereas the effect of adrenalin in this respect is but temporary. It will not take the place of salines, for on the latter rests the responsibility of maintaining the improvement produced by any remedy. The extract also causes powerful contractions in the pregnant, puerperal, and menstruating uterus. It probably acts better on an atonic organ than on a normal one. The remedy can be employed in a normal labor. **Subinvolution** due to the defective contraction and retraction is one of the dangers in **Cesarean section,** especially if performed before the onset of labor; in such circumstances secretions and blood-clots may be retained and become infected—a state of affairs favored by any contraction of the pelvis which may be present, for this condition leads to a sagging forward of a subinvoluted organ. The remedy ought to be given, but rarely before delivery. For general post-partum purposes it is better than ergot. It also excites active peristalsis in the bowel. There is little doubt that its chief effect is peripheral, for if we place a rabbit's isolated and active uterus in Ringer's solution the organ contracts violently on the addition of a small quantity of the extracts. W. H. Bell (Brit. Med. Jour., Dec. 4, 1909).

In 3 cases of **heart-failure** during **anesthesia** the writer injected 1 c.c. of a 20 per cent. solution of the posterior lobe of the pituitary body intramuscularly. The effect was almost immediate, and the almost imperceptible pulse soon became large and bounding. This effect lasted from twelve to sixteen hours, and gradually passed off. Not only did the pulse become larger in expansion, but it was also slowed, and, whereas it had been irregular, it became regular. This effect seems due not only to the action of the drug on the blood-vessels, but also on the heart. The injection was given in conjunction with normal saline by rectum. G. G. Wray (Brit. Med. Jour., Dec. 18, 1909).

The benefit which follows the use of pituitrin by intramuscular injection when the blood-pressure is abnormally low is very marked. The writer recommends it especially for **threatened collapse** and **hemorrhage after childbirth.** He thinks it may prove of value in **surgical shock** and in **acute febrile states,** but his use of it in these cases has not yet been extensive. Pituitrin has two advantages over adrenalin: namely, its action is moderate and prolonged. Klotz (Münch. med. Woch., May 23, 1911).

Obstetrics.—Dale found, in the course of comprehensive experiments,

that (in keeping with that of the adrenal principle) the action of extract of pituitary was "a direct stimulation of involuntary muscle without any relation to innervation." Fröhlich and Frankl-Huchwart then ascertained that it caused contractions of the pregnant uterus in rabbits, while Foges and Hofstätter resorted to this property in so far as the human uterus was concerned to check post-partum and other uterine hemorrhages, the test including 63 cases. The extract proved worthless by the mouth; but when injected intramuscularly, marked uterine contraction appeared within five minutes and lasted a long while in most cases.

S. J. Aarons found pituitary extract (vaporole) superior to ergot in **labor** cases. The uterus contracted better, more quickly, and more persistently than under ergot. It should not be used, however, until after completion of the third stage of labor, with the possible exception of certain cases of placenta prævia. The author gives brief histories of 11 illustrative cases. Among these is one of **placenta prævia** in which, after version and expulsion of the fetus, removal of the placenta was accompanied by **profuse hemorrhage.** An intra-uterine douche of weak bichloride of mercury at 120° F. (48.9° C.) was given and pituitary extract injected deeply into the buttock; after this, there was no further loss and the uterus remained well contracted. Several cases of normal labor followed by **hemorrhage** or **relaxation of the uterus** in which the extract gave good results are also cited.

In 63 cases of **post-partum hemorrhage** and after 1 **abortion** the intramuscular injection of pituitrin (in doses of 1 to 2 c.c.) proved superior to ergotin with reference to the intensity of the contraction and continuance of the excitability. The authors were enabled to note the effect of pituitrin particularly in 6 cases of extraperitoneal Cesarean section. "After not more than five minutes one could see how the exposed uterus contracted, in response to a light tactile irritation, to a firm ball. The action continued for a long time, which accounts for the fact that there was no hemorrhage, a complication that is always feared in connection with Cesarean section." In accordance with their observations, the authors are of the opinion that there is no doubt concerning the specific effect of pituitrin upon the excitation of the uterus. Foges and Hofstätter (Zentralbl. f. Gynäk., Nu. 46, 1910).

Five cases of **insufficiency or absence of labor pains;** from 0.6 to 1.3 grains of pituitrin were injected subcutaneously. In every case the result was remarkable. Within a short time the action of the uterus was normal and exhibited no tetanic character. This was especially noticeable during the period of expulsion. It is noteworthy that the writer obtained the same effect after a repetition of the pituitrin injection that followed the first administration of the remedy. The writer confirmed his clinical observations by means of animal experiments on the puerperal uterus of rabbits; a few minutes after the injection there were active contractions of the uterus, as was demonstrated by means of a delicate scientific apparatus. J. Hofbauer (Zentralbl. f. Gynäk., Nu. 4, 1911).

The writer has found pituitrin useful not only in **endometritis, metritis,** and **menorrhagias** which were, perhaps, dependent on increased ovarian activity, but also in **hemorrhages caused by inflammatory diseases of the adnexa, myomata, and ovarian cysts.** He uses the remedy subcutaneously in doses of 2 or 3 c.c. The only by-effect noticed was an occasional uterine cramp. Bab (Münch. med. Woch., July 18, 1911).

Case of a primipara in the difficult breech presentation showed signs of

nephritis, ischuria, amaurosis, and anasarca. No benefit being derived from quinine and ergot, pituitary extract was injected the third day on account of persisting ischuria and the delivery was forcibly completed with great difficulty. After a few hours of improvement the patient succumbed to the uremia. This suggests that pituitary should be reserved for uncomplicated uterine atony. Pfeifer (Zentralbl. f. Gynäk., June 3, 1911).

Pituitrin, the extract of the posterior lobe, stimulates the uterus to contract. The writers recommend its use whenever it becomes necessary to induce **premature labor.** The dose used by him is 0.6 to 1 c.c. (6½ to 15 grains) injected subcutaneously and repeated as often as necessary. During labor, the pains are almost invariably intensified and the child is born without showing any effects of the drug. To induce labor, as in tuberculosis and nephritis, repeated injections are often necessary, as the pains induced at first are not always of long duration or sufficient intensity. In 2 cases labor was terminated by the use of pituitrin alone; in a third it was also necessary to stretch the cervix. Even with advanced nephritis, the mothers showed no undesirable after-effects and the infants were perfectly normal. R. Stern and O. Bondy (Berl. klin. Woch., Aug. 7, 1911).

In 3 cases of **intestinal paresis** following operations for **ovarian cyst** and **ectopic gestation,** quite prompt relief was obtained by injections of pituitary extract. In a case of **subinvolution of the uterus,** the patient suffering from menorrhagia, for which she had recently been curetted without result, and having soft, flabby tissues and low blood-pressure, Aarons decided to try the effect of repeated doses of pituitary extract. Six injections were given in as many weeks. The uterus underwent contraction from 5 to 3 inches as measured by the sound; the general condition was much improved, and had remained so six months after the treatment. During the administration of the pituitary extract marked polyuria was noted. No deleterious effects resulted. The author suggests, however, that the use of the extract in subinvolution be limited to cases with associated low blood-pressure.

Ott and Scott found infundibulin, *i.e.,* extract of the posterior lobe, to act as a powerful **galactagogue** in the goat. So far, however, it has not been tried in women.

Infectious Diseases.—In this general class of disorders the use of pituitary acts, from my viewpoint, and in keeping with the effects of adrenal preparations, by enhancing the immunizing activity of the blood and the tone of the cardiovascular system. That such was the case in the infectious diseases in which it was tried can only, however, be surmised.

Rénon and Delille found that in **typhoid fever** it raised the blood-pressure, slowed the pulse, increased diuresis, and improved the patients in general, hastening convalescence noticeably. In **diphtheria,** in which the toxin reduces the vascular tension and promotes cardiac complications, it lowered the pulse rate, raised the blood-pressure, and increased diuresis. In **erysipelas** it seemed to hasten the favorable evolution of the disease. In **pneumonia** it raised the blood-pressure when this became low, but without influencing favorably the evolution of the disease. In **bronchopneumonia,** however, the opposite proved to be the case, considerable benefit being noted. **Influenza** was found to be very favorably influenced,

rapid recovery resulting in patients aged, respectively, 80 and 63 years. This was confirmed by Azam, in the infectious form. Rénon and Azam enumerate the phenomena which, in infectious diseases, indicate the need of pituitary: 1, a fall of the arterial tension; 2, quickening of the pulse and, as complementary minor phenomena, insomnia, anorexia, abnormal sweating, and heat flushes. Under the influence of pituitary there occur: 1, increase of arterial tension; 2, slowing of the pulse, with increase of power and amplitude; 3, increased diuresis; 4, increase in weight; 5, hastening of convalescence.

In several cases of tuberculosis treated by Rénon and Delille, the results were not, on the whole, encouraging. In a case of **Addison's disease** complicating tuberculosis, however, there was a notable rise of the blood-pressure and diminution of the asthenia. Trerotoli had already noted the beneficial effects of pituitary body in **Addison's disease**—a fact which further suggests that the active agent of pituitary substance is its adrenal component.

Exophthalmic Goiter.—Rénon and Delille obtained considerable improvement in this disease by the use of pituitary gland. From the fourth to the fifth day, the sleeplessness, tremor, digestive disturbance, sweating, and sensation of heat were considerably lessened. The tachycardia improved less rapidly, the pulse becoming slower gradually and attaining its slowest rate toward the fifteenth day. The arterial tension also rose steadily, attaining the maximum toward the third week, falling again somewhat, but not to the former low level. Some diminution of the exophthalmus occurred, but the goiter was not reduced. The dose administered was 4½ grains (0.30 Gm.) of the whole pituitary (ox) gland daily, a dose which they deem advisable to increase to 7½ grains (0.50 Gm.) in divided doses daily. The symptoms tend to return, however, on discontinuing the remedy. Cases subsequently treated were also benefited, but no cures were effected.

This mode of action, from my viewpoint, corresponds precisely with that referred to under the preceding heading. We have seen that the main pathological condition—that to which all the prominent symptoms of exophthalmic goiter were due—was a general dilatation of the arterioles. Pituitary extract causing constriction of these vessels as long as it is administered, it offsets for the time the morbid phenomena enumerated. That such is actually the case was demonstrated by Hallion and Carrion, who found, experimentally, that pituitary extracts "always produced their effects by raising the arterial tension," producing at the same time "an intense vasoconstrictor action upon the thyroid body." Briefly, we have here precisely the physiological action necessary, the vasoconstrictor power of the adrenal component of the pituitary gland superseding the vasodilator action of the thyroid, the underlying cause of the disease.

Nervous and Mental Diseases and Myopathies.—Rénon and Delille used pituitary in 10 **neurasthenics** in whom tachycardia; irregular vascular tension, often below normal; a sensation of oppression, myasthenia, insomnia, and anorexia were present. In these cases 3 to 5 grains (0.2 to 0.3 Gm.) daily proved remarkably useful, though no complete recovery was noted.

Delille and Vincent obtained a com-

plete recovery in a grave case of **bulbospinal myasthenia** by the simultaneous use of pituitary and ovarian extracts. Parhon and Urechia and Léopold-Lévi and de Rothschild had also obtained favorable results with pituitary in similar cases. Browning observed good effects in cases of **chorea** in which this disorder occurred in conjunction with **stunted growth,** as shown under the next heading.

In epilepsy it was tried by Mairet and Bose, but only served to increase the number of attacks—a result to be expected, since Spitska has shown that these were due to abnormal elevation of the blood-pressure. In some instances it provoked delirium.

Sollier and Chartier tried pituitary in **mental disorders** and found it useful in depressive states. It raised the blood-pressure, reduced the pulse, suppressed profuse sweating, and improved the asthenia. The synthesis of perceptions and the association of ideas were improved, and mental operations were incited more promptly.

Stunted Growth and Imbecility.—In a case in which a child of 3 years had shown the evidences of **hypothyroidia** with **idiocy** sufficiently to suggest the use of thyroid, Léopold-Lévi and de Rothschild found this agent useless. The case being attended with marked **myasthenia,** they administered pituitary extract, 1½ grains (0.1 Gm.) twice daily, which corresponded with 7½ grains (0.5 Gm.) of the fresh gland. Marked signs of improvement appeared within a few days. The intelligence developed to a remarkable degree, and soon reached that of a child of a corresponding age, 3 years, though before the treatment it did not exceed that of a 7 or 8 months' infant. Two similar cases, one of which showed symptoms of Little's disease, were similarly benefited.

Browning used pituitary only in **undersized** or **backward children and youths** (not real dwarfs or midgets). He gives the following histories:—

1. A frail, choreic girl of 14 years had made little or no recent advance in growth. On pituitary, with some accessories for the chorea, she gained a couple of pounds in weight and over an inch in height in three and a half months, the chorea disappearing. 2. A slightly rachitic boy of 2 years, after a period of cessation of growth, increased from 25 to over 30 pounds (*i.e.*, over 20 per cent.) in six months on the somewhat irregular administration of pituitary—besides recovering in all ways, and keeping up his good progress since, though at a slower rate. Browning noted when growth is once started up in this way it usually keeps on satisfactorily. 3. A somewhat choreic boy of 13 years and of scanty physique received pituitary, besides at times arsenic and accessories. Although his growth was said to have been at a standstill previous to this, he gained 2 inches in height and 10 pounds in weight in the next eight months. In another ten months, on somewhat irregular continuation of the pituitary, he made a further gain of 3 inches in height and 11 pounds in weight—when the father began to inquire anxiously for agents with the opposite effect. This is a record for a year and a half of 5 inches in height and over 20 pounds in weight, the patient having been under 56 inches and 70 pounds at the start.

Intestinal Paresis.—Bell and Hicks have found pituitary extract of value in paralytic distention of the intestines.

It never failed either in postoperative or other paresis if given intramuscularly when the intestine begins to distend in 15-minim doses (0.92 c.c.), repeated in an hour if required. The effect is then sustained by daily doses if need be. The beneficial influence of the injections was, as a rule, noticeable in a few minutes.

Pituitary body is a reliable agent for the treatment of **paralytic distention of the bowel.** In some respects the preparation is far ahead of adrenalin, apart from its greater efficiency and more prolonged action on the involuntary muscle-fibers, especially of the heart and kidneys. After a short initial increase in the frequency, the extract slows the heart and causes more powerful contraction, whereas adrenalin causes acceleration. While adrenalin causes a diminution in the secretion of the urine, infundibular extract has a marked diuretic effect, which is of very great postoperative value. There is also reason to believe that the extract may prove to be even more effective than adrenalin in producing local anemia. W. B. Bell (Brit. Med. Jour., Dec. 4, 1909).

Twenty-one cases illustrating the fact that pituitary extract has a very marked effect upon the muscular coats of the bowel, and that it is able to overcome the **temporary paralysis due to exposure after abdominal operations.** This is shown by the early passage of flatus and by the absence of abdominal discomfort. In only 3 cases did the bowels act without the assistance of the enema, but in every case except 2 a satisfactory action of the bowels was obtained after a simple enema, and it was necessary to give any aperient by the mouth. All the patients passed flatus freely within a few hours of the first injection, and were free from any abdominal pain or distention; no patient complained of flatulence. The flatus was often passed freely without the introduction of a flatus tube. The pulse rate remained much lower than usual, and after some of the severest operations it did not exceed 80 per minute. Except in the last 2 cases no patient suffered from postoperative retention of urine, and so catheterization was unnecessary. The patients treated with injections of pituitary extract after abdominal operations are certainly more generally comfortable than those who do not receive them. L. A. Bidwell (Clinical Journal, Sept. 6, 1911).

We have seen under the caption "Obstetrics" that pituitary gland was also of value in the intestinal paresis following pelvic operations.

ORCHITIC OR TESTICULAR ORGANOTHERAPY; SPERMIN.

The mode of action of these agents has not as yet been explained otherwise than by the process I have suggested, viz., that it is similar to that of the adrenal products, owing to the presence in these preparations of the adrenal principle.

That the testicle influences powerfully the organism at large is well shown by the fact that castration before puberty modifies in many particulars the development of the individual. They preserve to a certain extent the characteristics of infantilism, the skin remaining soft and white, their muscles flabby and weak, and the voice high-pitched. Yet they are usually tall, owing to inordinate growth of the bones. They lack courage, initiative, and intelligence. It is evident, therefore, that the testicles do not solely carry on genital functions. Brown-Séquard, in fact, taught that they carried on a dual rôle: 1, procreation; 2, the production of an internal secretion which stimulates and sustains the energy of the nerve-centers and cord, and capable, moreover, of endowing the individual with physical, moral, and intellectual char-

acteristics of sex. His own physical and intellectual activity having been greatly improved at the age of 72 years, by injections of an extract prepared from the testes of young dogs, he concluded that it possessed marked therapeutic value. No one who, as I did, saw Brown-Séquard before and after he had submitted himself to this treatment could stretch his imagination sufficiently to attribute the change in his appearance to autosuggestion. He literally looked twenty years younger. Unfortunately, the value of testicular preparations was exaggerated by many observers to such a degree that their use fell into disrepute, and the subject has received but little attention in recent years.

The prevailing opinion at the present time is that the beneficial effects obtained from testicular preparations are not due necessarily to an internal secretion, though the existence of such is not denied, but to nucleoalbumins, substances that are rich in phosphorus, resembling greatly lecithins and glycerophosphates.

> Up to the present time no reliable evidence is forthcoming to show that orchitic injection has any action other than that due to its nucleoalbumin, a substance, of course, which cannot be liberated into the blood-stream. The writer does not hint that there is the slightest doubt of the existence of an internal secretion, but only that its nature is as yet quite unknown to us. W. E. Dixon (Brit. Med. Jour., Sept., 21, 1907).

A personal analytic study of the question brought out a suggestive fact, viz., that "spermin," which may be obtained not only from testicles, but from the ovaries of mammals and fish roes, presents the characteristics of the adrenal secretion, both as to composition and physiological action. As I pointed out in 1903 (see "Adrenal Extract," *supra*), the adrenal secretion serves to take up the oxygen of the air and carry it to all parts of the body as the active constituent of hemoglobin. As such it sustains oxidation and metabolism. Now, Batty Shaw ("Organotherapy," 1st ed., p. 205, 1905) writes: "Spermin possesses the very curious property of being an oxygen carrier, and, according to Poehl, is responsible for those internal oxidations which take place in the body-tissues. Again, I have urged that the adrenal secretion carries on its oxygenizing function catalytically as a ferment. Pantchenko (reprint from Trib. médicale, 1896) states that "spermin acts catalytically, thus increasing the oxidizing power of the blood, and simultaneously activates the intraorganic oxidation processes where these are weakened." Moreover, as is the case with the active adrenal secretion, spermin gives the guaiac and Florence hemin test (Mari); it is, as a constituent of orchitic extract, unaltered by boiling (Dixon); it increases the force and regularity of the heart much as does digitalis (McCarthy); it enhances the resistance to disease; it increases the production of urea; it acts directly upon the cardiovascular system. Moreover, as shown by Poehl—a fact which indicates that it is not specific to the testis—it is a ubiquitous constituent of the whole organism, in the female as well as the male.

> Abnormalities in the frequency and rhythm of the pulse are benefited by a spermin when 20 drops are given three times a day. Its power of correcting irregular action of the heart depends on the fact that it is an active promoter of physiological tissue oxidation, espe-

cially in the case of neurin, xanthin, and other metabolic products which act as cardiac poisons, but are by oxidation converted into inactive compounds. G. von Hirsch (Trans. Congress of Intern. Med., Berlin, 1901).

Experiments upon animals showing that Poehl's spermin increases the volume of the blood-stream supplying the heart, thus increasing the "coefficient of blood supply of the heart." Spermin acts more energetically in this respect than the testicular emulsion of Brown-Séquard. The action of spermin depends upon its specific effect on the smooth muscle-fibers of the cardiac vascular system, and is almost independent of the muscular tone of the heart muscle and of the heart's action itself. Spermin acts but faintly upon normal hearts, but more markedly upon weakened hearts. Spermin should be used, therefore, in cases of diseased heart muscle and in autointoxications which give rise to a spasmodic narrowing of the cardiac vessels. Prozhanski (Roussky Vratch, Nov. 18, 1906).

Poehl having found in 1895 (Zeit. f. klin. Med., Bd. xxvi, H. 1 u. 2) that spermin was present in all the different parts of the organism, it becomes a question whether its actual source is the testicle, as believed by him, or whether, as I hold, it is derived from the adrenals, the testicles being richly supplied with it only because of the importance of their functions, *i.e.*, procreation. The relative importance of both sets of organs to life answers this question. If, as Poehl says, "it is the oxidizing action of spermin which plays the principal rôle in the phenomena it produces," the organs whose removal arrests oxidation sufficiently to render life impossible must be the source of the oxidizing agent. As is well known, removal of the testicles does not kill, while death invariably follows extirpation of both adrenals. It is plain, therefore, that the testicles do not produce the oxidizing substance shown by Poehl and others to be the active agent in spermin, and that it is the oxygen-laden adrenal secretion (adrenoxidase) it contains which endows it with therapeutic properties.

On the whole, the foregoing facts have shown that, while, as held by Dixon, orchitic extract is a compound of phosphorus-laden bodies, nucleins, lecithin, etc., which acts much as do glycerophosphates and similar products (though containing spermin in relatively small quantities), spermin owes its beneficial effects to the fact that it is rich in oxygenized adrenal secretion, *i.e.*, the product I have termed adrenoxidase.

THERAPEUTICS.—The fact that testicular preparations, including spermin, have been recommended in a large number of disorders has not served to recommend them to the impartial observer. The use of orchitic extract was extolled in various nervous disorders, especially **tabes, neurasthenia, melancholia, impotence,** and **paralysis agitans**; in several cutaneous disorders, **eczema** and **psoriasis**; in disorders of nutrition, **gout, obesity,** and **glycosuria**; but others again have failed to obtain any favorable results. Spermin has also been recommended by Poehl and his followers not only in the majority of the foregoing disorders, but in many others besides, in **acne, rheumatism, syphilis, marasmus,** and in various infections, such as **typhoid fever, diphtheria,** and even **cholera.** It has been tried in **Addison's disease,** but adrenal preparations are to be preferred.

In the light of the analysis submitted above, however, there is good ground for the belief that beneficial effects were obtained in all these mala-

dies. That the nucleoalbumins of orchitic extract, acting as would glycerophosphates, could be beneficial in the disorders enumerated, no one can deny. This can hardly be said, however, of the cutaneous and nutritional disorders, unless the spermin the extract contains, by enhancing oxidation and the destruction of toxic wastes, proves to be the active agent. Spermin itself—as adrenoxidase—is unquestionably capable of doing this actively, and in **syphilis** and **marasmus** to markedly enhance the functional activity of all tissues. Again, the beneficial rôle of spermin in **infections** finds its explanation in a fact I have repeatedly emphasized, viz., that the oxygenized adrenal secretion, the active agent of spermin from my viewpoint, is an active participant in all immunizing processes, local and general.

The main point to determine, however, is whether orchitic extract or spermin affords better or as good results in any of the disorders enumerated than other remedies at our disposal. The evidence available indicates that such is not the case. Hence, the disuse into which the testicular products have fallen.

OVARIAN ORGANOTHERAPY.—The ovaries correspond in many ways with the testes in their influence upon general development: their removal in children causes them to grow up without feminine attributes; absence of these organs prevents development of the uterus and the appearance of menstruation; their removal after puberty arrests menstruation and leads to atrophy of the genital organs. These phenomena were attributed by Curatulo, in accord with Brown-Séquard's doctrine, to the loss of what influence an internal secretion supplied by the ovaries to the body at large possessed over its development. The administration of ovarian substance in subjects deprived of their ovaries or during the menopause produced a marked amelioration of all distressing phenomena. This was found to be particularly the case by Régis, of Bordeaux, in the insanity and other morbid symptoms which occasionally follow operative removal of the ovaries.

The manner in which ovarian extract produces its effects has remained obscure. As Wilcox ("Pharmacology and Therapeutics," 7th ed., p. 824, 1907) says: "But little is known of its pharmacological action. Fresh ovarian extract is said, when injected into the circulation in rabbits, to raise the blood-pressure, diminish the heart's action, and slow the respiration, and when administered to the human female also to increase the arterial tension. In the castrated animal it is found to increase oxidation to somewhat above the normal degree, but on the normal animal it has no such effect." These are the identical effects produced by adrenal preparations. From my viewpoint, it is, in fact, owing to the presence of this substance—not necessarily an internal secretion—in the ovaries that they must be attributed. There exists, as shown by Schäfer, a close homology between the interstitial of the ovary and the same cells in the adrenals; both sets of organs are derived from the Wolffian body; ovarian extract raises the blood-pressure and slows the heart, as shown by Federoff, Jacobs, and others. Removal of the ovaries, moreover, reduces the oxygen intake 10 per cent., as shown by Loewy and Richter, while ovarian extract restores it; it has been, therefore, regarded as an oxidizing ferment. Neumann and Vas

noted that ovarian extract enhanced metabolism; Senator observed that ovarian preparations increased diuresis and the excretion of urea and phosphoric acid. Its physiological effects are those of adrenal preparations, therefore, in every respect.

Its effects on oxidation are so striking, in fact, that they have been clearly recognized by many clinicians. "We are authorized to classify ovarian organotherapy among the oxidizing agents," write Dalché and Lépinois. "This conclusion, it must be admitted, is that reached by several authors. Curatello and Tarulli believe that the internal secretion of the ovaries favors the oxidation of phosphorized organic substances, hydrocarbons, and fats. According to Gomes, it enhances oxidation and hydrolysis and favors the elimination of phosphates. . . . Albert Robin and Maurice Binet have shown that there is during menstruation an increase of the respiratory exchanges. Keller, studying the general exchanges, found that there was increased nitrogen oxidation. We have ourselves found that menstruation, in itself, enhances vital functions and particularly the great function of general oxidation."

> Ovarian extract causes an excretion of the phosphates, which is less marked in women whose ovaries have been removed. In general, castration appears to diminish the salts in the body. Mathes (Monats. f. Geb. u. Gyn., Bd. xviii, H. 2, 1904).
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> The ovary appears to preside in some way over the metabolism of inorganic matter, and, hence, aids in maintaining the composition of the blood. Thus when young bitches are castrated there is an initial reduction of the number of erythrocytes and amount of hemoglobin. Offergeld (Deut. med. Woch., June 22, 29, 1911).

PREPARATIONS AND DOSES.—The preparation in general use is the *desiccated gland,* available in the form of 2-grain tablets, which may be given in doses of 2 to 4 grains (0.132 to 0.26 Gm.) twice daily. The *fresh organ* may be employed in 10- to 15- grain (0.6 to 1.0 Gm.) doses where the pharmaceutical product is not available. As the patient becomes readily habituated to the remedy, it is best to begin with small doses and to increase them gradually. It owes its action to the corpus luteum it contains.

THERAPEUTICS.—As in the case of testicular preparations and spermin, ovarian extractives have been tried in a multitude of disorders with more or less benefit or without any whatever.

Natural and Artificial Menopause.—In disorders occurring in the course of the **physiological menopause,** or when the latter is produced by bilateral oöphorectomy, ovarian preparations have proven of considerable value in a large proportion of cases since Brown-Séquard first introduced their use. Experience has shown, however, that the improvement lasts only as long as the agent is administered, and that, furthermore, certain phenomena: the palpitation, trembling, and "nervousness," disappear earlier than the others, *i.e.,* the asthenia, flushes, irritability, and psychoses, though effects in all symptoms, including the cutaneous disorders—especially acne rosacea and eczema—are promptly realized, sometimes as early as the fourth day.

These effects are normally explained by the influence of the remedy on general oxidation and the improvement of the antitoxic functions of the blood, the imperfect hydrolysis of tissue wastes being the underlying cause of the phenomena other than the general asthenia.

The best results are obtained in young women who have grown obese after removal of the ovaries, or in whom **obesity** is due to ovarian insufficiency. In physiological menopause they are less marked, as a rule, and sometimes fail altogether to appear. In such instances, good results may sometimes be obtained by giving simultaneously 1 grain (0.066 Gm.) desiccated thyroid, or by depending upon the latter remedy alone. In the **amenorrhea** of congenital ovarian insufficiency, desiccated ovary has caused the appearance of menstruation.

W. E. Dixon, of Cambridge University, recalls that the presence of ovarian tissue in the body, however small in amount, is sufficient to prevent the distressing symptoms which frequently follow complete extirpation; even transplanted ovaries are sometimes able to prevent the menopause attending removal of the ovaries. Hence, the beneficial effects of ovarian preparations.

Improvement has also been obtained by some observers in **acne, prurigo,** and **eczema.** They have been found to cause an increase of the red corpuscles in **chlorosis** and to afford benefit in **gout, epilepsy, exophthalmic goiter** and **obesity,** and also in **dysmenorrhea.**

Of late, however, the general attention has been centered upon the therapeutic use of the essential structure of the ovary, the corpus luteum.

CORPUS LUTEUM ORGANOTHERAPY.

The consensus of opinion at the present time is that the internal secretion of the ovary is produced by the corpus luteum. The function of the corpora lutea in the early stages of their life is to initiate growth processes in the uterine cavity by means of this internal secretion and subsequently to preside over the nidation and development of the ovum, and the cyclic engorgement preceding menstruation. The recent labors of Fraenkel confirming his previous investigations have strongly sustained the internal secretion theory and its controlling influence over the above functions. He found, moreover, that the therapeutic value of corpus luteum was limited to cases presenting symptoms of vasomotor origin due to absent or deficient ovarian activity.

This coincides with the earlier conclusion of J. G. Clarke that the office of the corpus luteum was, among others, that of "a preserver of the ovarian circulation"—a fact which explains in turn the presence of adrenal-like tissue, whose secretion, as is well known, is eminently capable of sustaining vascular tone. Indeed, as is generally believed, it is the corpus luteum which produces the ovarian internal secretion; it should, in accord with what I have stated concerning the mode of action of the ovaries, also produce effects similar to those of adrenal preparations. We need but recall that in the adrenal hypernephroma of children one of the essential phenomena witnessed is the extraordinary development of the genital organs, those of a child of 5 years, for instance, being practically those of an adult. Bouin, Ancel, and Villemin found that the primary effect of toxic doses of lutean extract was a violent elevation of the blood-pressure, sufficient to produce effusion into all serous cavities. The physiological effects of therapeutic doses have not been sufficiently studied to show positively, as was the case with the ovaries, that they are all those of adrenal preparations, though what there is known points in that direction. One

fact is certain, however, viz., the functions of the organ should not be ascribed to its internal secretion; its mission is probably limited to that of sustaining the ovarian circulation, as pointed out by J. G. Clarke.

On the whole, from my viewpoint, the physiological action of corpus luteum, in organotherapy, is that of ovarian substance (*q.v.*), which, in turn, as we have seen, is mainly that of adrenal substance in organic combination.

PREPARATIONS AND DOSES.—The preparations available include desiccated corpus luteum (*glandulæ lutei desiccatæ*), which may be given in 3- to 5- grain (0.2 to 0.3 Gm.) doses three times daily. It is usually administered before meals, but if, as is sometimes the case, it causes gastric disturbances it may be administered during, that is to say, in the course of, the meal. The term "lutein" is sometimes applied to the same product, but it is misleading, and its use should be discouraged.

THERAPEUTICS.—The indications for desiccated luteum are similar to those for ovarian preparations.

Natural and Postoperative Menopause and Disorders of Pregnancy.—It must be said that the evidence as to the therapeutic value of desiccated luteum is, to say the least, conflicting. Morley, who supplied desiccated luteum to ten physicians, and obtained reports of its use in 18 cases, 14 of which suffered from **postoperative menopause**, and 4 from **natural menopause**, states that 5 were cured, 12 improved, and that but 1 failed to be relieved.

C. A. Hill also reported results obtained with extract of corpora lutea in 12 patients, ranging in age from 25 to 38 years, who showed the most severe type of nervous symptoms after removal of both ovaries. The "nervousness" was completely relieved by the treatment in each case. In only 2 cases, however, was there complete relief from flashes of heat. In another case, suffering from insomnia, which had continued ever since the operation over a year before, and was uninfluenced by hypnotics, complete relief was attained after the use of 50 5-grain (0.33 Gm.) capsules. One case reported an increase in sexual desire, while in the remainder no noticeable change was experienced. No complete cures were obtained. Several cases had interrupted treatment only, and others, who ceased treatment, were compelled to resume owing to return of symptoms. The preparation in each case was given in 5-grain (0.33 Gm.) capsules three times daily, one-half to one hour before meals.

On the other hand, Ellice McDonald publishes a report of 20 personal cases in which he had used a similar preparation. "The results of this study, small though they be, extending over five years," writes this observer in his conclusions, "seem to indicate that the control of surgical menopause need not be sought in the corpora lutea. Its value is in cases in which the uterus and ovaries or uterus alone are retained. Particularly is it valuable in the treatment of **scanty menstruation** and the **premature menopause**. I have treated a number of cases at the outdoor dispensary of the Kensington Hospital for Women, with extract of the whole ovary, and never saw any definite results therefrom. But the lutein extract, being the essential part of the ovary, does seem to help in some degree and should be

accompanied, in suitable cases, by dilatation of the uterus, with the use of the stem pessary following operation, as advised by Manson. At least, administration of lutein is indicated after operations on pregnant women in whom **miscarriage** is feared. This is particularly true in the early weeks of pregnancy during the imbedding of the ovum, as it has been shown experimentally that the corpus luteum has a definite effect under such circumstances." There is also some ground for the belief that it will prove of some value in **osteomalacia** and in **agalactia**, *i.e.*, as a galactogogue.

> The consensus of opinion seems to be that the internal secretion of the ovary is produced by the yellow body. The extract may be given in 5-grain doses, three times a day, from one-half to one hour before meals. The writer's results in 18 cases were as follows: 5 were cured, 12 were improved, and 1 obtained no relief. Included in these 12 are grouped those who are still taking the extract. A permanent cure may result in a few of those under treatment. Of the 18 patients, 14 suffered from disturbances of operation or **artificial, and** 4 from those of natural or **physiologic menopause.** Morley (Jour. Mich. State Med. Soc., Nov., 1909).
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> The extract of human corpus luteum possesses a distinct therapeutic action in **osteomalacia,** disturbances of the **natural and artificial menopause,** and in hypofunction due to **infantile uterus.** In **amenorrhea** and in **dysmenorrhea** the treatment must at first be given each month. Maits (Univ. of Penna. Med. Bull., July-Aug., 1910).
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> In experiments upon the goat with the glands containing internal secretions, the writers found that the thymus and corpus luteum increase the quantity of milk fourfold in five minutes. The ovary minus corpus luteum has no effect. Infundibulin is still the most powerful **galactogogue,** increasing the secretion of milk one hundredfold. The amount of butter fat is about the same in the augmented secretion by thymus, corpus luteum, and infundibulin, though occasionally it is increased. Ott and Scott (Mo. Cyclo. and Med. Bull., Feb., 1911).

It is obvious that the clinical experience at our disposal is still too limited to warrant any decision as to the actual value of corpus luteum, though it must be said that many desultory cases have been published in which its rise was extolled. McDonald rightly lays stress on the facts that "the manifestations of the surgical menopause are too varied and extreme to allow explanation by the mere absence of the internal secretion of the ovary. The internal secretion of the ovary is but a factor in the process of the menstrual life."

I would go one step farther and express a doubt that we are dealing at all with an "internal secretion," a designation applied to almost any organic juice nowadays, and reiterate what I say elsewhere, viz., that true internal secretions are fewer than is generally believed.

KIDNEY ORGANOTHERAPY.

Brown-Séquard, having removed the kidneys and caused uremia, found that the injection of a glycerin extract of kidney prolonged the life of the animals as compared to those in which the same operation was not followed by the use of the kidney extract. This experiment, which has been repeated by others, forms the basis of the belief that the kidney produces an internal secretion. That such a conclusion may not be warranted is suggested by the fact that the kidneys, along with some of the organs so far reviewed, are also rich in adrenal tissue—the so-called "adrenal rests" from hypernephroma some-

times develops—and that as such they are capable, as an active factor in the immunizing functions of the body, of counteracting temporarily the toxemia or "uremia" brought on by removal of the kidneys. Indeed, the relief afforded is but ephemeral, death being postponed but one or two days in rabbits, in which Bitzou repeated Brown-Séquard's experiments. Dromain and de Pradel Bra had also noticed that injections of kidney extract lessened the fits of epilepsy, another toxemia. Dubois and Renaut have already, in fact, attributed antitoxic power to kidney extracts.

That we are again dealing mainly with a manifestation of the adrenal principle is further suggested by its powerful blood-pressure-raising property. Tigerstedt and Bergman found that rennin possessed this power; Bingel and Strauss recently confirmed their observation, and found that its action corresponded with that of adrenal and pituitary extracts, those of other organs causing depressor effects. The use of pressure produced by kidney extract was high, *i.e.*, from 40 to 60 mm. Hg, and lasted from fifteen to thirty minutes. The authors concluded, moreover, that "the action of rennin, like that of adrenalin, is exerted in the muscles of the peripheral vessels." Its general action, however, is more like that of pituitary body extract, the adrenal principle being doubtless combined organically, as in the pituitary, with bodies which prolong and perhaps control advantageously the action of the former. Like adrenal preparations kidney extract also produces myosis.

Even the oxidizing power I have attributed to the adrenal secretion seems to be reproduced; Batty Shaw, who also finds "very little justification for the existence of an internal secretion" in the kidney, remarks that "possibly nephrin and other renal preparations provide a means of stimulating oxidation in general, the kidney merely sharing in this oxidation"—a very accurate estimate from my viewpoint. Shaw adds, moreover, that "similar good results have been reported as a result of treatment by means of spermin and testicular extract," both of which, as I have shown, also owe, in all probability, their therapeutic effects to the adrenal principle they contain.

THERAPEUTICS AND DOSE.—The therapeutic application of kidney preparations has received considerable attention, and favorable results have been reported in about one-half of the cases of **chronic nephritis**, or **Bright's disease**, in which it was tried. The mode of action, in the light of the facts submitted above, is mainly an increase of the antitoxic power of the blood and diminution, therefore, of the irritation of renal apparatus. Page and Dardelin, for example, report marked amelioration in 18 cases, using a maceration prepared as follows: A very fresh kidney from a pig is cut into minute pieces, washed with fresh water to remove the excess of urine, then hashed and pounded into pulp. This pulp is put into 300 Gm. (9 ounces and 5 drams) of fresh water to which the physiological proportion of salt, 7.50 to 1000, has been added. It is then allowed to macerate for three hours, stirred occasionally, and kept in a cool place to avoid fermentation. The red water of the maceration is divided into three parts, to be drunk by the patient during the day. It is more conveniently given, however, in tablet form, as "nephritin," prepared in this country by Reed and Carnrick. Only the active

substance of the kidney is used in this preparation, the dose being from 10 to 15 5-grain (0.33 Gm.) tablets daily in divided doses, given between meals.

Kidney preparations have also been used with more or less advantage in **puerperal intoxications** and **epilepsy**, but their field is essentially the various forms of nephritis, and particularly for the prevention of **uremia**. They also tend to increase diuresis and reduce the albumin. As stated above, however, favorable effects are to be expected in about one-half of the cases.

THYMUS ORGANOTHERAPY.

In 1907, I submitted evidence which had led me to suggest that the function of the thymus was to supply an excess of phosphorus in organic combination during the growth of the body, *i.e.*, particularly while the development of the osseous and nervous systems demanded such a reserve. This was sustained by the recognized fact that certain diseases of children and adolescents, especially marasmus, rachitis, and trophic disorders of the brain and nervous system, were due, in part, to the functions of the thymus. While it cannot be affirmed that this theory actually represents the function of the organ—the thymus having been the graveyard of many hypotheses—all that can be said for it is that it seems to account for the clinical results obtained under its use better than any hypothesis so far advanced, besides corresponding with the laboratory findings of its effects.

THERAPEUTICS.—Diseases of the Thyroid.—In **simple goiter** it was first tried by Mikulicz, who obtained sufficiently favorable results in 5 out of 11 cases to render operation unnecessary, at least for the time being. Reinbach considers it probably superior to thyroid because the unpleasant effects of the latter are avoided; for the same reason it is especially suitable when organotherapy has to be used continuously. This view is based on the employment of thymus in a large number of cases in the Breslau clinic. Mikulicz gave from 2½ to 4 drams (10 to 16 Gm.) of the raw sheep thymus on bread three times a week, increasing the dose slightly if required.

In **exophthalmic goiter** it had proven efficacious in the hands of Owen in advanced cases, and also in those of Mande when other remedies had been used fruitlessly. The latter gave 45 grains (3 Gm.) daily to a severe case, which greatly improved, relapsing whenever the treatment was interrupted. S. Solis-Cohen also advocates its use in this disease, having found that it exerted its beneficial influence mainly upon the nervous symptoms of the disease without affecting the exophthalmus. Huston White found that the nervous symptoms were alone improved.

These observations coincide with my own view of the manner in which thymus gland produces its beneficial effects. The excess of thyroiodase produced in exophthalmic goiter causes, we have seen, too rapid oxidation of the phosphorus in organic combination in the tissues, particularly in those of the nervous system, which are extremely rich in phosphorus. Thymus, supplying phosphorus in organic combination, replaces that lost by the nervous system, thus procuring marked benefit in this one direction. As 5 grains (0.33 Gm.) of the dried thymus are equivalent to 30 grains (2 Gm.) of the fresh gland, this dose can readily be given three times daily.

Rachitis, or Rickets.—The same ex-

planation, *i.e.*, the purveying of phosphorus in organic combination—to the osseous system, in the present connection—accounts for the undoubted benefit thymus has procured in this disorder. Mendel, having used thymus gland in 1½ to 3 drams (6 to 12 Gm.) daily in over 100 cases, obtained marked benefit in a large proportion, but especially in the nervous symptoms, including spasm of the glottis. It had previously been tried by Stoppato, but without marked benefit. In Mendel's cases both fresh and commercial tablets were tried, the cases being subdivided as follows: 1, those which showed prodromal symptoms only; 2, those in which deformity of the osseous system was the chief feature; 3, those marked by spasm of the glottis, and, 4, those in which splenic enlargement was the most important sign. Marked improvement was noted in all after from three to four weeks, and dentition and the closure of the fontanelle proceeded satisfactorily. No untoward symptoms were noted—a marked advantage over thyroid preparations. In a case of **stunted growth**, obviously of osseous origin, in a boy of 14 years, R. Webb Wilcox obtained 9¼ inches growth in three years by the persistent use of 2 grains (0.13 Gm.) thymus night and morning.

The view that these effects are due to the addition of phosphorus in organic combination to the body is further sustained by the results of experimental observation by Hart and Nordmann, that the thymus had a definite relation to assimilation, and that it took an active part in the resistance of the organism to infection. As my own investigations have shown (see the second volume of "Internal Secretions," page 878), nucleoproteid, in so far as its phosphorus in organic combination is concerned, is an active participant in the immunizing process.

> Great relief, particularly from the **pain of cancers**, can be attained by the use of thymus extract. This line of treatment was originally worked out by Gwyer, who showed that in cases where the treatment was tried there was marked decrease, or even elimination, of pain. The glands used were received fresh. The fat was removed, and the glandular substance cut up and dried at a low temperature by a forced draught of air, then ground and sifted to a uniform powder. Of this a dose of from 1 to 4 drams was given three or four times a day. Gwyer also prepared a watery extract from the dried gland by adding the dried powder and some thymol to a solution of normal saline, straining and filtering as rapidly as possible, filtering twice, and then adding 50 per cent. acetic acid. The precipitate so obtained was separated by filtration and redissolved, using about 1½ ounces of the solution. Each dram of the solution represents the products from half a dram of the dried gland. The process for the production of an ounce of the extract takes about six hours. This fluidextract is administered either by mouth or hypodermically up to 1 dram. Takaki (Hospital, Jan. 21, 1911).

BONE-MARROW ORGANOTHERAPY.

The bone-marrow being the source of red corpuscles, its preparations have been tried in **pernicious anemia, the secondary anemias, chlorosis, malaria, leucocythemia, leukemia, Hodgkin's disease, rickets,** and other disorders of the osseous system. In all of these affections bone-marrow gave good results in some cases, while an equal number were in no way influenced. This obviously suggests that its indications coincide with certain phases or stages of the disease which have not

as yet been determined. The average dose is 5 grains, after meals.

BRAIN AND NERVE SUBSTANCE ORGANOTHERAPY.

The belief, based on pure assumption, that brain and nerve substance possess or produce an internal secretion has never been sustained scientifically.

The clinical results, though quite discordant, particularly in the neuroses and psychoses in which these preparations have been tried, have shown a tendency to harmonize since the introduction by Sciallero of an oily extract. Page, who has obtained unusually good results in **neurasthenia** by means of injections of this extract, ascribes them to its antitoxic and antispasmodic effects. Wassermann and Takaki had previously shown that **tetanus** toxin was neutralized by contact with brain substance, and that when a fatal dose of tetanus toxin was injected with brain substance the fatal effects were prevented. The same observations were made in the case of **hydrophobia** by Babes; in **strychnine** and **morphine poisoning** by Widal and Nobécourt; in tetanus by Krokiewicz; in **epilepsy** by Lion, and also Kaplan, using Poehl's opocerebrin—in accord with Dana's experience several years earlier. Sciallero, who obtained encouraging results in **neurasthenia, hysteria, chorea, tic,** and **epilepsy,** used his oily extract "cephalopin" in doses varying from 1 to 5 c.c. (16 to 81 minims). No untoward effects were obtained.

Although it is very improbable that brain extracts injected into the tissues act as they do in the test-tube, it seems established that they act much as do the lecithins on the market, *i.e.,* by furnishing phosphorus to the organism in an assimilable form, or as nucleoproteids in enhancing the immunizing process. Be this as it may, these substances seem to have produced effects which suggest that they should, not as yet, be set aside.

MAMMARY GLAND ORGANOTHERAPY.

It is held by some that the mammary gland produces an internal secretion; but the evidence is so scant that it can hardly be taken into account.

> There are various indications that the mammary gland may be the source of an internal secretion. Ovarian insufficiency, for example, is often accompanied by congestive or painful phenomena in the breasts. Again, the mammary gland can compensate for another organ. Thus, Djemil Pacha, after removing two hypertrophied breasts from a man, witnessed the development of marked cachexia strumipriva in his patient. Apert, Léopold-Lévi, and de Rothschild have also observed the concomitant presence of gynecomastia with hypothyroidia. The purpose of the mammary secretion would seem to be, however, that of acting as antagonist to that of the ovaries. Luncz (Revue médico-chirurgicale, Aug. 1, 1911).

Although mammary gland, introduced by Bell, of Glasgow, and in the United States by the late John H. Shober, has been used considerably, and has shown a marked stimulating action upon the uterus, the manner in which it produces this effect has remained obscure. An extract lowers somewhat, and but temporarily, the blood-pressure and the pulse. According to Shober, it diminishes the blood supplied to the uterus and thus controls hemorrhage, its action resembling that of ergot, though free of the unpleasant effects of the latter drug.

Mammary gland is prepared in the form of a tablet made of the desiccated gland of the sheep, each tablet repre-

senting 20 grains (1.32 Gm.) of the fresh gland. The dose is from 3 to 6 tablets daily.

The therapeutic application is restricted to the genital apparatus. In cases of **uterine fibroids** characterized by excessive **menorrhagia** and **metrorrhagia** the bleeding was found by Shober to be controlled in a few weeks and the periods become regular, normal, and free from pain. There is improvement in the patient's health and weight, and the tumors themselves diminish in size up to a certain point. In 43 cases treated by Fedoroff, complete cure occurred in one-third, *i.e.*, 33 per cent.; a reduction of volume in 43 per cent., and no result whatever in 14 per cent. The hemorrhages disappeared completely in 80.3 per cent. of the cases. According to Fedoroff, the best effects are obtained when the mammary extract is used hypodermically. The patient is thus placed in a better condition for any needed operation, and often the necessity for an operation is postponed. Where there is evidence of inflammatory or degenerative changes, or when serious pressure symptoms are not controlled after a reasonable trial, operation should not be delayed. The mammary gland is also useful in cases of **subinvolution** unassociated with malignancy or structural changes.

Mammary gland has also given good results, in the hands of Pozzi, in the uterine hemorrhages attending **metritis** of any kind. It decongests the organ and thus counteracts inflammation.

It has also been recommended to assist **uterine involution** and to enhance lactation in **agalactia**. Here, again, the results reported have been antagonistic. The dose is 5 grains (0.32 Gm.), repeated several times daily, preferably after meals.

SPLEEN ORGANOTHERAPY.

This is based mainly on the prevailing opinion that the spleen destroys red corpuscles and creates new ones, and that it produces some sort of immunizing body, its leucocytes, as in lymph-glands, being phagocytic.

Extracts of spleen have been tried in various disorders, including **exophthalmic goiter**, the **secondary anemias, pernicious anemia, chlorosis, lymphadenoma,** and **leucocythemia,** but the results have not been such as to warrant further trial. Bayle recommends it highly in **tuberculosis.**

> The writer considers spleen tissue or extract as a specific for **tuberculosis.** He gives 100 Gm. of raw pork spleen tissue daily for three weeks and recommences again each time after an interval of two weeks. It is readily taken in soup or preserves, he says, or extracts of the spleen may be used. He commenced this treatment about 1903, and now has a record of 150 patients with pulmonary tuberculosis and 21 with bone or joint tuberculosis, all given a systematic course of spleen organotherapy, with a complete cure in 75 per cent. of the patients, only 4 not showing marked benefit under it. Joly has also cured 93 per cent. of his 90 patients. All the local processes heal under this treatment ten times faster, the writer urges, than is the case under any other methods of treatment. It is readily applied and causes no febrile reaction and no evil effects. Bayle (Revue de méd., June, 1911).

Pancot, Carpenter, and others claim to have obtained good results from splenic extract in the treatment of **malaria.** Lemansky found that it enhanced the action of quinine.

HEPATIC ORGANOTHERAPY.

Besides the functions carried on by the bile, which will be referred to below, the liver subserves several useful rôles. It is endowed with important

antitoxic functions, all foodstuffs absorbed through the intestinal mucosa entering the organ through the portal system for this purpose. It supplies, out of the glycogen it forms, the blood and tissues the sugar they contain; it takes part in the metabolism of nitrogenous substances and forms urea. That these many phases of usefulness should have suggested the use of hepatic substance is not surprising. Gilbert and Carnot found it useful in various conditions.

In **diabetes** liver extract was found to act with considerable energy; in some cases, however, the sugar was promptly diminished, even to *nil* occasionally, while in others it increased it. I have called attention to the fact that two forms of diabetes, the sthenic and asthenic, should be clearly distinguished from each other, the treatment of one form being pernicious in the other. It is in the asthenic form that hepatic extract will be found of value. Lereboullet has also observed beneficial effects in some cases.

> Cases in which the administration of liver substance brings about improvement are those in which the **diabetes** is connected with a functional inadequacy of the liver (characterized by diminution of urea, urobilinuria, etc.). On the other hand, cases of diabetes that are not benefited or are even made worse by the treatment are those in which the glycosuria appears to depend on overactivity of the organ. Gilbert (Inter. Congress of Med.; Brit. Med. Jour., Oct. 13, 1900).

One important feature of liver therapy is that, as emphasized by practical experience, the remedy causes diuresis in subjects who suffer from **hepatic insufficiency** in some form and particularly when it occurs in the course of **cirrhosis.** The diuresis is also accompanied by increased urea elimination.

> Case of **cirrhosis of the liver** with abundant edema and ascites; the liver was small, the spleen much enlarged, and the collateral circulation very marked. The patient was put upon a milk diet and given about 4 ounces of fresh pork liver mixed with bouillon. Abdominal puncture resulted in the withdrawal of 4 quarts of fluid besides what oozed from the wound during several days following. The urine was rapidly increased to over 90 ounces a day; this is considered a valuable prognostic sign. Gradually the edema and the collateral circulation disappeared and there was no return of the ascites. Unfortunately, the results in all cases are not so favorable as in this. M. Hirtz (La presse médicale, No. 52, p. 413, 1904).
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> Case of **tuberculous peritonitis** and **cirrhosis of the liver** which when first seen presented general anasarca, dyspnea, albuminuria, and hematuria. After being treated four months, during which time tapping was often necessary, irrigations of 10 ounces of a pulp made from pigs' liver were prescribed. In less than two months there was marked improvement: the hematuria was less, tapping was no longer necessary, and the masses in the peritoneum had decreased in size. The patient continued to improve rapidly and returned to work. The writer reports a second similar instance in which just as remarkable a cure was attained. Desplats (Jour. de sci. méd. de Lille, No. 30, p. 73, 1905).
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> Case of **atrophic cirrhosis with ascites.** On admission paracentesis was performed and about 7 quarts of fluid withdrawn. Seven hours later a second tapping seemed necessary, but hepatic extract was prescribed instead. Marked and rapid diuresis resulted, and the general state of the patient became much improved. This form of treatment, according to the observer, should give excellent results in the precirrhotic stage of this disease. J. Carles (Revue de thérapeutique, No. 11, p. 387, 1906).

In a case of **cirrhosis** of long duration in which the daily excretion of urine did not exceed 450 Gm., ten days' treatment with hepatic extract raised the flow to a quart (1000 Gm.) and more. Interruption of the treatment caused resumption of oliguria, soon followed by death. Cases of marked diuresis after the use of hepatic extract have been reported by many authors, Gilbert and Carnot, Widal, Hirtz, and others. M. Perrin (Paris médical, Dec. 16, 1911).

In **alcoholic cirrhosis** it was also found of value by Gilbert and Carnot. The edema, jaundice, and hemorrhages were kept in abeyance in a case reported, returning whenever the use of liver extract was interrupted.

The coagulating action of liver on the blood, shown by Gilbert and Carnot, was carefully studied by Berthe. The patients on whom the observations were made were tuberculous, and had suffered repeatedly from **hemoptysis,** which had not responded to any ordinary treatment. In all cases the results were rapid. The method was also tried in cases of **epistaxis** and **metrorrhagia.** The method consisted in giving an extract of liver, about 3 drams (12 Gm.) for a dose, in tepid soup. This amount will in many cases suffice, but can be repeated when necessary. It can also be administered per rectum in the same dose. One of the best and most suitable preparations is the *desiccated liver.* The *glycerin extract* is also efficacious. Should it not be possible to procure a ready-made extract, an *emulsion* of liver freshly prepared, and given in the form of an enema, seems to act perfectly well, 3 to 6 ounces (94 to 186 Gm.) being finely chopped up and then rubbed up with water, about 4½ ounces (140 Gm.) of liver being used. Fresh pigs' liver is one of the best sources of preparation.

Liver extract, now available on the market, has also been used with advantage in **chronic gastrointestinal intoxication,** the object being to check the growth of bacterial flora. Biliary acids, referred to below, are, however, preferable. A convenient way is to use the biliary extract in suppositories.

While liver extract gives uncertain results in diabetes, its use in the form of suppositories night and morning is of positive value in chronic **gastrointestinal autointoxication,** a relatively common disorder. O. L. Mulot (Long Island Med. Jour., Dec., 1910).

BILE, BILE-SALTS, AND BILIARY EXTRACTS.

The use of *bile* in therapeutics is based on a sounder basis than that of several of the foregoing agents, its excitomotor action on the intestine, now fully demonstrated, serving various useful purposes. It counteracts constipation due to intestinal atony, and thus prevents autointoxication of intestinal origin, which, in turn, produces cholangitis by allowing the return into the portal system of excretory products which should have escaped normally with the intestinal discharges. Again, bile, as shown by Pawlow, is a physiological auxiliary to the pancreatic juice, augmenting its activity threefold. As is well known also, bile, or gall, increases the solubility of cholesterin, thus preventing the formation of gallstones. Bile is also endowed with antitoxic properties.

Series of experiments upon rabbits consisting of direct injection into the exposed gall-bladder of bacteria of various species and virulence. The bile was found to contain some substance which interfered with the development of most varieties of colon, typhoid, and diphtheria bacilli, the different bacteria varying greatly in their susceptibility to the unfavorable influence of the bile.

The bactericidal action of the bile varied at different times and with different animals. One of the most important factors influencing the result of the injections was the number of bacteria that reached the bile passages. The liver-cells and the epithelial cells of the bile passages strongly resisted any attempt at entrance on the part of bacteria; this was particularly striking with diphtheria bacilli. S. Talma (Zeit. f. klin. Med., Bd. xlii, Heft 5 u. 6, 1901).

In 101 specimens of bile, organisms were recovered in 8 cases, and, from 12 calculi, organisms were recovered in six instances. The organisms observed most frequently were of the colon type. In 37, pure cultures of the colon bacillus were obtained, and, in association with other organisms, *Bacillus coli* was observed 35 times. The typhoid bacillus was recovered in two instances: one in which typhoid fever had existed thirteen years previously, and in the second instance from a person dying as a result of typhoid perforation. A large Gram-positive bacillus was also found in 26 cases. This organism was morphologically and tinctorially identical with the *Bacillus aërogenes capsulatus.* This organism developed abundantly in the bouillon cultures where colon and other organisms developed. Williams (N. Y. Med. Jour., May 13, 1911).

The therapeutic use of bile or bile constituents is thus based on a solid foundation. They may be used as stated above, in **constipation** and **putrefaction** due to hepatic and intestinal atony, **autointoxication** of intestinal origin, in **cholangitis** and the resulting **jaundice,** and also to prevent the formation of **gall-stones.** They have also been used advantageously in **enterocolitis** in its membranous form.

Study of 15 cases from a metabolic standpoint which seem to indicate that the administration of bile in certain conditions is based upon rational therapeutics. Consequently, the writers advocate the administration of bile in **jaundice** due to various causes. Absorption of fat is increased; it also has a laxative effect. The writers give inspissated oxbile in sweetened aromatic water in doses of from 0.5 to 1 Gm. one hour before meals. Given with considerable water it will not disturb gastric digestion. Inouye and Sato (Arch. f. Verdauung-Krank., Bd. xvii, 185, 1911).

Mucomembranous enterocolitis and **constipation** being the result of insufficiency of the biliary secretion, their treatment becomes simple. The general indications are: (1) reduction to a minimum of the quantity of toxic and putrefactive products in the intestine by an appropriate diet; (2) shortening of the period of transit of food through the alimentary canal and prevention of the coagulation of mucus by the use of a cholagogue, the best of which is bile itself. The writer uses an extract devoid of putrescible nucleoalbumins, which he has termed *antimucose,* available in 0.20-Gm. (3.1 grains) dragées; suppositories, and ampules of 50 c.c. (1.7 fluidounces) in which the biliary substances, dissolved in water, occur in the concentration of normal bile. H. Nepper (Monthly Cyclopedia and Med. Bull., Jan., 1912).

Although cholic acid is the most active of the bile-salts, salts of glycocholic or taurocholic acid are preferred. They possess all the therapeutic properties of oxgall. The *sodium glycocholate* or *taurocholate* can be conveniently used in ½- to 3- grain (0.032 to 0.19 Gm.) doses three times a day. Or, the *extract of bile* may be given in 5- to 15- grain (0.32 to 1.0 Gm.) doses after meals, with a draught of water. Bile may also be injected into the rectum to cause its evacuation. This is especially valuable in **paralytic ileus, postoperative** and **peritonitic atony,** or **paresis** of the **intestine** from any cause.

Bile acids may be employed with propriety chiefly in three conditions: **intestinal putrefaction, hepatic insufficiency, gall-stone disease,** and the various syndromes known to be consecutive to these states. The writer employs glycocholic acid, in the form of the sodium salt, because it is more readily procurable and cheaper than taurocholic acid. The dose varies according to the exigencies of the case. The writer has been in the habit of giving ½-grain doses at frequent intervals until the desired effect is produced. There is never any danger of giving too much because the sodium glycocholate in no way deranges the stomach, and, if given in very large doses, merely occasionally produces a little diarrhea, which promptly carries off the surplus. Croftan (N. Y. Med. Jour., April 2, 1906).

The preferred preparation is the extract of oxgall, the minimum dose of which is from 7½ to 15 grains administered in pill form after meals. In extreme instances it may be necessary to give as large a quantity as 75 grains, but such doses should not be continued. The pills should be coated with keratin or similar substances, so that their contents may not be set free until they reach the intestine. The patient should be advised to drink more than the usual amount of water in order that the increased quantity of bile which is excreted as a result of the medication may not become inspissated. M. Nigay (Revue de thérap., 387, 1906).

Bile administered per rectum leads to prompt evacuation of the bowels, peristalsis, as shown by studies in dogs, being set up chiefly in the large intestine. Bile acids are the active constituents of the bile. Cholic acid acts most powerfully, though taurocholic and glycocholic acids also cause active peristaltic movements. Because of the expense, the extensive use of cholic acid is precluded. "Platner's" bile has been found to be a suitable substitute, given in doses of 0.2 to 0.5 Gm. As a rule, the patient has a stool in five to fifteen minutes after administration per rectum. The stool is formed with no excess of fluid. Glaessner and Singer (Wien. klin. Woch., Bd. xxiii, S. 5, 1910).

HORMONES.

Bayliss and Starling termed "secretin" a hormone formed in the duodenal mucous membrane under the influence of hydrochloric acid from the stomach. Carried by the circulation to the intestinal mucosa, the pancreas, and the liver, it activates the production of the secretions produced by these organs. From my viewpoint, as I suggested in 1907 ("Internal Secretions and the Principles of Medicine," vol. ii, p. 861), this hormone presents several properties of adrenal extractives. Be this as it may, the question has not been sufficiently developed as yet to warrant any conclusion as to the exact mode of action of these substances.

Another hormone, however, has been obtained from the gastric mucosa by Zuelzer, Dohrn, and Marxer (Berl. klin. Woch., Nu. 46, 1908) which has been found to enhance peristalsis. It being impossible to obtain it in sufficient quantities from the stomach, it was sought after elsewhere, and was found in ample quantities in the spleen—that junkshop in which red corpuscles (which, as I suggested in 1903, are the common carriers of the adrenal principle) are broken up along with other cells. This splenic hormone specifically stimulates intestinal peristalsis to a degree so remarkable that the intestinal movements in the experimental animal may readily be shown cinematographically ten to fifteen minutes after an intravenous injection.

This hormone (available as *hormonal* in the trade) has been found of considerable value in **chronic constipation,** intravenous injections (20 c.c.—5

drams) giving 71 per cent. of recoveries, beginning from the second to the seventh day and lasting from six months to two years (Zuelzer). The injection gives but little local pain thus used, and causes a slight rise of temperature (hormone fever). In **intestinal paralyses** following abdominal operations or volvulus it has also given satisfactory results in some cases.

> Series of 6 cases of grave **intestinal paralysis** which had resisted all other means. Hormone injections caused general improvement and the emission of gas in from one to five hours after the injection. But the effect did not seem to be lasting. It is advisable to enhance the action by means of enemata and purgatives to insure the elimination of the intestinal contents. Henle (50th German Congress of Surgery, April, 1911).

In **intestinal occlusion** the use of hormones has been recommended, but care is necessary lest the violent peristalsis provoked aggravate any intestinal lesion that may be present.

> The writers recall that four years before Zuelzer did so they isolated the substance which in the intestinal mucosa promotes peristalsis, and to which the term "peristaltic hormone" was subsequently applied. Enriquez and Hallion (C.-r. de la Soc. de Thérapeutique, Oct. 25, 1911).

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